```
L11
    ANSWER 1 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
     2007:619959 CAPLUS
                         Full-text
DN
     147:52917
ΤI
     method for treatment of an ocular neovascular disorder by administration
     of 5-[[4-[(2,3-dimethyl-2H-indazol-6-yl)methylamino]-2-pyrimidinyl]amino]-
     2-methylbenzenesulfonamide and (S)-3-oxo-8-[3-(pyridin-2-ylamino)-1-
     propyloxy]-2-(2,2,2-trifluoroethyl)-2,3,4,5-tetrahydro-1H-2-benzazepine-4-
     acetic acid.
ΙN
     Brigandi, Richard Anthony; Levick, Mark; Miller, William Henry
PΑ
     Smithkline Beecham Corporation, USA
SO
     PCT Int. Appl., 49pp.
     CODEN: PIXXD2
DT
     Patent
ĹΑ
     English
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                   DATE
                                            ______
PΙ
     WO 2007064752
                          Α2
                                20070607.
                                            WO 2006-US45776
                                                                   20061129
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
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             MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
             RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRAI US 2005-740478P
                                20051129
                          ·P
     A method for treating an ocular neovascular disorder comprises administration
AB
     of 5-[[4-[(2,3-dimethyl-2H-indazol-6-yl)methylamino]-2- pyrimidinyl]amino]-2-
     methylbenzenesulfonamide (Pazopanib) and (S)-3-oxo-8-[3-(pyridin-2-ylamino)-1-
     propyloxy]-2-(2,2,2-trifluoroethyl)- 2,3,4,5-tetrahydro-1H-2-benzazepine-4-
     acetic acid or salts or solvates thereof. Pazopanib (multistep preparation
     given) in a mouse model reduced choroidal neovascularization in a dose-
     dependent manner.
IT
     205678-26-8P
```

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(treatment of ocular neovascular disorder by administration of dimethylindazolylmethylaminopyrimidinylaminomethylbenzenesulfonamide and oxopyridinylaminopropyloxytrifluoroethyltetrahydrobenzazepineacetat e)

205678-26-8 CAPLUS RN

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)-, (4S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 205676-70-6P

RL: PEP (Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)

(treatment of ocular neovascular disorder by administration of dimethylindazolylmethylaminopyrimidinylaminomethylbenzenesulfonamide and oxopyridinylaminopropyloxytrifluoroethyltetrahydrobenzazepineacetate)

RN 205676-70-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-2-methyl-3-oxo-, methyl ester (CA INDEX NAME)

IT 205676-79-5P 205676-80-8P

RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (treatment of ocular neovascular disorder by administration of dimethylindazolylmethylaminopyrimidinylaminomethylbenzenesulfonamide and oxopyridinylaminopropyloxytrifluoroethyltetrahydrobenzazepineacetate)

RN 205676-79-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-, methyl ester, (4R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 205676-80-8 CAPLUS

RN

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-, methyl ester, (4S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 205676-69-3P 205676-71-7P 205677-80-1P 205677-81-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(treatment of ocular neovascular disorder by administration of dimethylindazolylmethylaminopyrimidinylaminomethylbenzenesulfonamide and oxopyridinylaminopropyloxytrifluoroethyltetrahydrobenzazepineacetate) 205676-69-3 CAPLUS

CN Butanedioic acid, 2-[[4-methoxy-2-[(methylamino)methyl]phenyl]methyl]-, 1,4-dimethyl ester (CA INDEX NAME)

RN 205676-71-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-2-methyl-3-oxo-, methyl ester (CA INDEX NAME)

RN 205677-80-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-81-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)-(CA INDEX NAME)

Absolute stereochemistry.

```
ANSWER 2 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
     2006:1202261 CAPLUS Full-text
ΑN
DN
     145:495768
     Soft tissue implants, anti-scarring agents, and therapeutic compositions
ΤI
IN
     Hunter, William L.; Toleikis, Philip M.; Gravett, David M.; Maiti, Arpita;
     Liggins, Richard T.; Takacs-Cox, Aniko; Avelar, Rui; Signore, Pierre E.;
     Loss, Troy A. E.; Hutchinson, Anne; McDonald-Jones, Gaye; Lakhani, Fara
PA
     Angiotech International A.-G., Switz.
SO
     PCT Int. Appl., 2979pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 3
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                    DATE
PΙ
    WO 2006121521
                          Α2
                                20061116
                                            WO 2006-US11690
                                                                    20060331
    WO 2006121521
                          А3
                                20070111
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
             VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRAI US 2005-679293P
                          Ρ
                                20050510
     US 2005-679962P
                          Р
                                20050510
AΒ
     Soft tissue implants (e.g., breast, pectoral, chin, facial, lip, and nasal
     implants) are used in combination with an anti-scarring agent in order to
     inhibit scarring that may otherwise occur when the implant is placed within an
     animal.
ΙT
     205678-31-5, Sb-273005 ·
     RL: DEV (Device component use); PAC (Pharmacological activity); PEP
     (Physical, engineering or chemical process); PYP (Physical process); TEM
     (Technical or engineered material use); THU (Therapeutic use); BIOL
     (Biological study); PROC (Process); USES (Uses)
```

(soft tissue implants, anti-scarring agents, and therapeutic compns.)

1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-

pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX

NAME)

Absolute stereochemistry.

205678-31-5 CAPLUS

RN

CN

```
ANSWER 3 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
AN
     2006:1202260 CAPLUS Full-text
DN
     145:495820
ΤI
     Electrical devices, anti-scarring agents, and therapeutic compositions
IN
     Hunter, William L.; Toleikis, Philip M.; Gravett, David M.; Maiti, Arpita;
     Liggins, Richard T.; Takacs-Cox, Aniko; Avelar, Rui; Signore, Pierre E.;
     Loss, Troy A. E.; Hutchinson, Anne; McDonald-Jones, Gaye; Lakhani, Fara
PΑ
     Angiotech International A.-G., Switz.
SO
     PCT Int. Appl., 2278pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
FAN.CNT 3
     PATENT NO.
                         KIND
                                DATE
                                             APPLICATION NO.
                                                                    DATE
PΙ
     WO 2006121518
                          A2
                                20061116
                                            WO 2006-US11610
                                                                    20060331
     WO 2006121518
                          A3
                                20070111
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             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC.
             VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            'KG, KZ, MD, RU, TJ, TM
PRAI US 2005-679292P
                          Ρ
                                20050510
     US 2005-679293P
                          Ρ
                                20050510
     Elec. devices (e.g., cardiac rhythm management and neurostimulation devices)
AΒ
     for contact with tissue are used in combination with an anti-scarring agent in
     order to inhibit scarring that may otherwise occur when the devices are
     implanted within an animal.
ΙT
     205678-31-5, Sb-273005
     RL: DEV (Device component use); PAC (Pharmacological activity); TEM
     (Technical or engineered material use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (implants incorporating anti-scarring agents)
RN
     205678-31-5 CAPLUS
CN
     1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-
```

pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI)

Absolute stereochemistry.

NAME)

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L11 ANSWER 4 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
```

AN 2006:764538 CAPLUS Full-text

DN 145:262702

TI Small molecule drug activity in melanoma models may be dramatically enhanced with an antibody effector

AU Popkov, Mikhail; Rader, Christoph; Gonzalez, Beatriz; Sinha, Subhash C.; Barbas, Carlos F., III

CS Department of Molecular Biology and the Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, USA

SO International Journal of Cancer (2006), 119(5), 1194-1207 CODEN: IJCNAW; ISSN: 0020-7136

PB Wiley-Liss, Inc.

DT Journal

LA English

ABMonoclonal antibody (mAb) 38C2 belongs to a group of catalytic antibodies that were generated by reactive immunization and contains a reactive lysine. 38C2 catalyzes aldol and retro-aldol reactions, using an enamine mechanism, and mechanistically mimics natural aldolase enzymes. In addition, mAb 38C2 can be redirected to target integrins  $\alpha v\beta 3$  and  $\alpha v\beta 5$  through the formation of a covalent bond between a  $\beta$ -diketone derivative of an arginine-glycine-aspartic acid (RGD) peptidomimetic and the reactive lysine residue in the antibody combining site to provide the chemical programmed mAb cp38C2. In this study, we investigated the potential of enhancing the activity of receptor-binding small mol. drug (SCS-873) through antibody conjugation. Using a M21 human melanoma xenograft model in nude mice, cp38C2 inhibited the growth of the tumor by .apprx.81%. The chemical programmed antibody was shown to be highly active at a low concentration while SCS-873 alone was ineffective even at dosages .apprx.1,000-fold higher than those used for the chemical programmed antibody. In vitro programming of the catalytic antibody was shown to be as effective as in vivo programming. In an exptl. metastasis assay, treatment with mAb cp38C2 significantly prolonged overall survival of tumor-bearing severe combined immuno-deficient (SCID) mice when compared to treatment with unprogrammed mAb 38C2, SCS-873 alone or the integrin-specific monoclonal antibody LM609. In vitro, cp38C2 inhibited human and mouse endothelial and human melanoma cell adhesion, migration and invasion. Addnl., cp38C2 inhibited human and mouse endothelial cell proliferation and was active in complement-dependent cytotoxicity assays. These studies establish the potential of chemical programmed monoclonal antibodies as a novel and effective class of immunotherapeutics that combine the merits of traditional small mol. drug design with immunotherapy.

IT 518315-49-6, SCS-873

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(small mol. drug activity in melanoma models may be dramatically enhanced with an antibody effector)

RN 518315-49-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-[19-[[4-(3,5-dioxohexyl)phenyl]amino]15,19-dioxo-4,7,10-trioxa-14-azanonadec-1-yl]-2,3,4,5-tetrahydro-3-oxo-8[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A

Me—C—CH<sub>2</sub>—C—CH<sub>2</sub>—CH<sub>2</sub>—CH<sub>2</sub>

NH—C—(CH<sub>2</sub>)3—C—NH—(CH<sub>2</sub>)3—O—CH<sub>2</sub>—

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 5 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
           2006:627654 CAPLUS Full-text
AN
DN
           145:89995
ΤI
           Methods and formulations of vitronectin antagonists to prevent scarring
           Blake, Simon M.; Miller, William Henry; Sayani, Amyn; Wilkens, H. Jeffrey
ΙN
PA
           Smithkline Beecham Corporation, USA
SO
           PCT Int. Appl., 57 pp.
           CODEN: PIXXD2
DT
           Patent
LA
           English
FAN.CNT 1
           PATENT NO.
                                                       KIND
                                                                      DATE
                                                                                                APPLICATION NO.
                                                                                                                                                   DATE
                                                       ____
ΡI
           WO 2006069079
                                                         A2
                                                                      20060629
                                                                                                WO 2005-US46204
                                                                                                                                                   20051220
           WO 2006069079
                                                       A3
                                                                      20070419
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                            VN, YU, ZA, ZM, ZW
                    RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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                            CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
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                            KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
PRAI US 2004-637824P
                                                         Ρ.
                                                                      20041221
OS
           MARPAT 145:89995
            The present invention describes methods and formulations using vitronectin
            receptor antagonists for the prevention of excessive scarring.
ΙT
           205678-16-6
           RL: PEP (Physical, engineering or chemical process); PYP (Physical
           process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
           USES (Uses)
                  (methods and formulations of vitronectin antagonists to prevent
                 scarring)
RN
           205678-16-6 CAPLUS
CN
           1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-(2-benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-(2-benzazepine-4-acid, 2,3,4,5-tetrahydro-3-(2-benzazepine-4
```

pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

```
ANSWER 6 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ΑN
     2005:219703 CAPLUS Full-text
DN
     142:274008
TI
     Methods for treating rheumatoid arthritis by administration of humanized
     antibody to IP-10 alone or in combination with additional therapeutic
IN
     Lane, Thomas E.
PΑ
     USA
     U.S. Pat. Appl. Publ., 15 pp.
SO
     CODEN: USXXCO
DT
     Patent
     English
LA
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                    DATE
PΙ
     US 2005053600
                          Α1
                                20050310
                                            US 2004-938673
                                                                    20040909
     WO 2005023201
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     WO 2005023201
                          А3
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             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
PRAI US 2003-501312P
                                20030909
                          Ρ
     The invention discloses methods and compns. for treating rheumatoid arthritis
     through the administration of humanized anti-IP-10 antibody alone or in
     combination with an addnl. anti-rheumatic therapeutic compound Early treatment
     of type II collagen-induced mouse arthritis models with anti-IP-10 monoclonal
     antibody IP6C7 remarkably diminished paw swelling.
ΙT
     205678-31-5, SB273005
     RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
     THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (as addnl. agent; humanized antibody to IP-10 alone or in combination
        with addnl. therapeutic agents for treating rheumatoid arthritis)
RN
     205678-31-5 CAPLUS
```

1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-

pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX

Absolute stereochemistry.

NAME)

CN

```
ANSWER 7 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ΑN
     2004:902129 CAPLUS Full-text
DN
     141:388640
ΤI
     Nitrogen containing integrin targeting compounds
ΙN
     Tamiz, Amir; Bradshaw, Curt W.
PΑ
     Covx Pharmaceuticals, Inc., USA
SO
     PCT Int. Appl., 182 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                    DATE
ΡI
     WO 2004091542
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                                            WO 2004-US12034
                                                                    20040415
                          A3 .
     WO 2004091542
                                20050414
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             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
             SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
PRAI US 2003-463456P
                          Ρ
                                20030415
     US 2003-507887P
                          Ρ
                                20030930
OS
     MARPAT 141:388640
     The present invention provides integrin targeting compds. which comprise small
     mol. weight integrin targeting agent-linker conjugates which are linked to a
     polymer such as a protein. The integrin targeting compds. of the invention
     comprise an RGD peptidomimetic integrin targeting agent covalently linked to a
     polymer such as the combining site of an antibody. Various uses of the
     invention compds. are provided, including methods to prevent or treat cancer
     or other disease.
IT
     518315-49-6D, conjugates with mouse monoclonal 38C2 antibody
     RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (nitrogen containing integrin targeting compds. linked to polymers such as
        proteins and antibodies for treatment of cancer and other diseases)
RN
     518315-49-6 CAPLUS
     1H-2-Benzazepine-4-acetic acid, 2-[19-[[4-(3,5-dioxohexyl)phenyl]amino]-
CN
     15,19-dioxo-4,7,10-trioxa-14-azanonadec-1-yl]-2,3,4,5-tetrahydro-3-oxo-8-
     [3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)
```

PAGE 1-A

Me—C—CH<sub>2</sub>—C—CH<sub>2</sub>—CH<sub>2</sub>—CH<sub>2</sub>

NH—C—(CH<sub>2</sub>)3—C—NH—(CH<sub>2</sub>)3—O—CH<sub>2</sub>—

THU 782475-44-9D, conjugates with mouse monoclonal 38C2 antibody RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(nitrogen containing integrin targeting compds. linked to polymers such as proteins and antibodies for treatment of cancer and other diseases)

RN 782475-44-9 CAPLUS

CN

1H-2-Benzazepine-4-acetic acid, 2-[(16S)-16-[[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]amino]-39-[[4-(3,5-dioxohexyl)phenyl]amino]-15,19,35,39-tetraoxo-4,7,10,24,27,30-hexaoxa-14,20,34-triazanonatriacont-1-yl]-2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-C

L11 ANSWER 8 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:878370 CAPLUS Full-text

DN 141:366143

TI Preparation of alkoxyoxobenzazepinylacetates from the corresponding phenols prepared in turn from formylhydroxyphenylmethylidenesuccinates

IN Conde, Jose J.; Goldfinger, Lewilynn L.; Mcguire, Michael A.; Shilcrat, Susan C.; Wallace, Michael D.; Yu, Marvin Sungwhan

PA Smithkline Beecham Corporation, USA

SO PCT Int. Appl., 60 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.				KIND		DATE		APPLICATION NO.					DATE			
PI	WO 2004089890 . WO 2004089890			A2 A3		20041021 20050630		,						20040329			
	W:	AE, A	3, AL,	AM,	ΑT,	ΑU,	AZ;	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,	
		CN, CO															
		GE, G															
		LK, L															
		NO, N	Z, OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
		TJ, TI	1, TN.,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW	
	RW:	BW, G	H, GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	ΤZ,	UG,	ZM,	ZW,	AM,	ΑZ,	
•		BY, K	G, KZ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	
		ES, F	[, FR,	GB,	GR,	ΗŪ,	IE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	
		SK, T	R, BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	
		TD, TO															
				A2		2006	0301	EP 2004-758669									
	R:	AT, B	E, CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙT,	LI,	LU,	NL,	SE,	MC,	PT,	
		IE, S	[, LT,	LV,	FI,	RO,	CY,	TR,	BG,	CZ,	EE,	HU.,	PL,	SK			
	JP 2006	T	T 20060928									20040329					
	US 2006	A1	A1 20060831				US 2005-551710					20051003					
PRAI	US 2003-460535P			P 20030404													
	US 2004-546212P					20040220											
	WO 2004-US9909					2004	0329					•					
OS	MARPAT 141:366143													•			
GI																	

RFO 
$$CO_{2}H$$
 I  $CO_{2}R^{3}$  II  $CO_{2}R^{3}$  II  $CO_{2}R^{4}$  III  $CO_{2}R^{4}$  I

Title compds. [I; R1 = Q5, Q6, etc.; R2 = haloalkyl, (substituted) alkyl, alkenyl, alkynyl, oxoalkenyl, oxoalkynyl, aminoalkyl, aminoalkenyl, etc.; W = (CHRg)aU(CHRg)b; a, b = 0-2; m, n = 0, 1; Q1-Q4 = N, CRy;  $\leq$ 1 of Q1-Q4 = N; Ry = H, halo, cyano, NO2, CF3, (substituted) alkyl, etc.; U = null, CO, O, NRg, CO2, N:N, C.tplbond.C, etc.; Rg = H, alkyl, cycloalkylalkyl, aralkyl, heterocyclylalkyl; R' = H, alkyl, aralkyl, cycloalkylalkyl; R'' = R', COR',

CO2R'], were prepared from benzazepine-phenols (II; R2 as above; R3 = H, protecting group), which in turn were prepared from formylhydroxyphenylmethylidenesuccinates (III; R4, R5 = H, protecting group). Thus, Me [(S)-8-hydroxy-3-oxo-2-(2,2,2-trifluoroethyl)-2,3,4,5-tetrahydro-1H-benzo[c]azepin-4-yl]acetate (preparation given) in tert-Bu Me ether (TBME) was treated with 6-methylamino-2- pyridineethanol (preparation given) in TBME followed by Ph3P and diisopropyl azodicarboxylate in TBME under cooling followed by stirring at room temperature to give after saponification with LiOH 56% <math>(S)-(-)-8-[2-[6-(methylamino)pyridin-2-yl]-1-ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-1,2,4,5-tetrahydro-2- benzazepine-4-acetic acid.

IT 205678-16-6P 205678-26-8P 205678-31-5P 779349-64-3P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (preparation of alkoxyoxobenzazepinylacetates from the corresponding phenols prepared in turn from formylhydroxyphenylmethylidenesuccinates)

RN 205678-16-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

RN 205678-26-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)-, (4S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205678-31-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 779349-64-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

IT 205677-02-7P 205677-04-9P 205677-32-3P 773059-56-6P 779349-60-9P 779349-63-2P 779349-65-4P, Methyl 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-2-(2,2,2-trifluoroethyl)-1H-2-benzazepine-4-acetate 779349-67-6P 779349-68-7P 779349-69-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of alkoxyoxobenzazepinylacetates from the corresponding phenols prepared in turn from

formylhydroxyphenylmethylidenesuccinates)

RN 205677-02-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205677-04-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205677-32-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 773059-56-6 CAPLUS

CN Butanedioic acid, [(2-formyl-4-hydroxyphenyl)methyl]-, dimethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 779349-60-9 CAPLUS

CN Butanedioic acid, [[2-(dimethoxymethyl)-4-hydroxyphenyl]methyl]-, (2S)-, compd. with N-cyclohexylcyclohexanamine (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 779349-59-6 CMF C14 H18 O7

Absolute stereochemistry.

CM 2

CRN 101-83-7 CMF C12 H23 N

RN 779349-63-2 CAPLUS

CN Butanedioic acid, [[2-[[[(1,1-dimethylethoxy)carbonyl](2,2,2-trifluoroethyl)amino]methyl]-4-methoxyphenyl]methyl]-, (2S)-, compd. with N-cyclohexylcyclohexanamine (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 779349-62-1 CMF C20 H26 F3 N O7

Absolute stereochemistry.

CM 2

CRN 101-83-7 CMF C12 H23 N

RN 779349-65-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester (9CI) (CA INDEX NAME)

MeO-
$$C$$
- $CH_2$ 
OH
$$F_3C-CH_2$$

RN 779349-67-6 CAPLUS

CN Butanedioic acid, [[2-(dimethoxymethyl)-4-hydroxyphenyl]methyl]-, compd.

with N-cyclohexylcyclohexanamine (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 779349-66-5 CMF C14 H18 O7

CM 2

CRN 101-83-7 CMF C12 H23 N

RN 779349-68-7 CAPLUS

CN Butanedioic acid, [(2-formyl-4-hydroxyphenyl)methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 779349-69-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester (9CI) (CA INDEX NAME)

ANSWER 9 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

2004:811010 CAPLUS ΑN Full-text

DN -142:23498

ΤI Chemical Adaptor Immunotherapy: Design, Synthesis, and Evaluation of Novel Integrin-Targeting Devices

ΑU Li, Lian-Sheng; Rader, Christoph; Matsushita, Masayuki; Das, Sanjib; 'Barbas, Carlos F., III; Lerner, Richard A.; Sinha, Subhash C.

Skaggs Institute for Chemical Biology, Department of Molecular Biology, CS Scripps Research Institute, La Jolla, CA, 92037, USA

SO Journal of Medicinal Chemistry (2004), 47(23), 5630-5640 CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DTJournal

LA: English

CASREACT 142:23498 OS

ΑB A series of  $\beta$ -diketone derivs. of RGD peptidomimetics that selectively bind to  $\alpha v \beta 3$  and  $\alpha v \beta 5$  integrins were synthesized and covalently docked to the reactive. lysine residues of monoclonal aldolase antibody 38C2. The resulting targeting devices strongly and selectively bound to human cancer cells expressing integrins  $\alpha v\beta 3$  and  $\alpha v\beta 5$  as analyzed by flow cytometry. In vitro and in vivo studies revealed that these novel integrin-targeting devices efficiently inhibit tumor growth. Thus, the combination of  $\beta$ -diketone derivs. of RGD peptidomimetics that target cell surface integrins lpha v eta 3 and lpha v eta 5 with monoclonal aldolase antibodies through formation of a covalent bond of defined stoichiometry holds promise as a new approach to cancer therapy.

ΙT 801239-98-5

RL: PRP (Properties)

(mol. docking studies of RGD peptidomimetics binding integrin  $\alpha v \beta 3$ )

RN 801239-98-5 CAPLUS

1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-8-[2-[6-CN (methylamino) - 2-pyridinyl] ethoxy] - 3-oxo-, (4S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 518315-49-6P 801239-17-8P 801239-19-0P

801239-22-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of diketone derivs. of RGD peptidomimetics as antitumor agents and determination of their biol. activity towards integrins  $\alpha\nu\beta3$  and  $\alpha v\beta 5$ )

RN 518315-49-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-[19-[[4-(3,5-dioxohexyl)phenyl]amino]-15,19-dioxo-4,7,10-trioxa-14-azanonadec-1-yl]-2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

$$Me = C - CH_2 - C - CH_2 - C$$

PAGE 1-B

RN 801239-17-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-[15,19-dioxo-19-[[4-[3-oxo-3-(2-oxocyclohexyl)propyl]phenyl]amino]-4,7,10-trioxa-14-azanonadec-1-yl]-2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-(9CI) (CA INDEX NAME)

PAGE 1-B

RN 801239-19-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-[19-[[4-(3,5-dioxohexyl)phenyl]amino]-15,19-dioxo-4,7,10-trioxa-14-azanonadec-1-yl]-2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-(9CI) (CA INDEX NAME)

$$Me = C - CH_2 - CH_2$$

RN 801239-22-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-[19-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-15-oxo-4,7,10-trioxa-14-azanonadec-1-yl]-2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

IT 801239-28-1P 801239-30-5E 801239-84-9P
801239-85-0P 801239-86-1P 801240-04-0P
801240-05-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(preparation of diketone derivs. of RGD peptidomimetics as antitumor agents and determination of their biol. activity towards integrins  $\alpha v\beta 3$  and  $\alpha v\beta 5)$ 

RN 801239-28-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-(17,17-dimethyl-15-oxo-4,7,10,16-tetraoxa-14-azaoctadec-1-yl)-2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A

O
t-BuO\_C\_NH\_ (CH2)3\_O\_CH2\_CH2\_O\_CH2\_CH2\_O\_ (CH2)3\_

0---

HO2C-

PAGE 1-B

RN 801239-30-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[2-[6-[[(1,1-dimethylethoxy)carbonyl]methylamino]-2-pyridinyl]ethoxy]-2-(17,17-dimethyl-15-oxo-4,7,10,16-tetraoxa-14-azaoctadec-1-yl)-2,3,4,5-tetrahydro-3-oxo-(9CI) (CA INDEX NAME)

PAGE 1-A t-BuO\_C\_NH\_ (CH<sub>2</sub>)<sub>3</sub>\_O\_CH<sub>2</sub>\_CH<sub>2</sub>\_O\_CH<sub>2</sub>\_CH<sub>2</sub>\_O\_ (CH<sub>2</sub>)<sub>3</sub>\_O=

но2С-

RN 801239-84-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-2-(17,17-dimethyl-15-oxo-4,7,10,16-tetraoxa-14-azaoctadec-1-yl)-2,3,4,5-tetrahydro-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-B

RN 801239-85-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-(17,17-dimethyl-15-oxo-4,7,10,16-tetraoxa-14-azaoctadec-1-yl)-2,3,4,5-tetrahydro-8-hydroxy-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-B

RN 801239-86-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-(17,17-dimethyl-15-oxo-4,7,10,16-tetraoxa-14-azaoctadec-1-yl)-2,3,4,5-tetrahydro-8-[3-[(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-B

RN 801240-04-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-(17,17-dimethyl-15-oxo-4,7,10,16-

tetraoxa-14-azaoctadec-1-yl)-2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-B

PAGE 1-B

RN 801240-05-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[2-[6-[[(1,1-dimethylethoxy)carbonyl]methylamino]-2-pyridinyl]ethoxy]-2-(17,17-dimethyl-15-oxo-4,7,10,16-tetraoxa-14-azaoctadec-1-yl)-2,3,4,5-tetrahydro-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:668007 CAPLUS Full-text

DN 141:332034

TI Multi-Kiloscale Enantioselective Synthesis of a Vitronectin Receptor Antagonist

AU Wallace, Michael D.; McGuire, Michael A.; Yu, Marvin S.; Goldfinger, Lynn; Liu, Li; Dai, Wenning; Shilcrat, Susan

CS Synthetic Chemistry Department, GlaxoSmithKline, King of Prussia, PA, 19406, USA

SO Organic Process Research & Development (2004), 8(5), 738-743 CODEN: OPRDFK; ISSN: 1083-6160

PB American Chemical Society

DT Journal

LA English

OS CASREACT 141:332034

GI

The development of a novel, cost-effective synthesis of the vitronectin receptor antagonist SB-273005 (I) became necessary as the compound proceeded to Phase 1. A practical synthesis of the compound presented challenges to the process chemist. Chief among the challenges was developing an enantioselective route to the compound Second was either developing a scalable Mitsunobu coupling of the side chain to the main body or finding alternate chemical This paper describes the chemical which allowed the preparation of a hundred kilograms of SB-273005 by a process that is suitable for even larger scale manufacturing

IT 205677-04-9P. 773059-56-6P 773059-59-9P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (multi-kiloscale enantioselective synthesis of SB-273005 as a vitronectin receptor antagonist)

RN 205677-04-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 773059-56-6 CAPLUS

CN Butanedioic acid, [(2-formyl-4-hydroxyphenyl)methyl]-, dimethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 773059-59-9 CAPLUS

CN Butanedioic acid, [(2-formyl-4-hydroxyphenyl)methyl]-, (2S)-, compd. with N-cyclohexylcyclohexanamine (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 773059-58-8 CMF C12 H12 O6

## Absolute stereochemistry.

CM 2

CRN 101-83-7 CMF C12 H23 N

## NH

IT 205678-31-5P, SB-273005

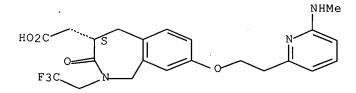
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(multi-kiloscale enantioselective synthesis of SB-273005 as a vitronectin receptor antagonist)

RN 205678-31-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX NAME)

## Absolute stereochemistry.



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L11
     ANSWER 11 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ΑN
     2003:991468 CAPLUS Full-text
DN
     140:27670
ΤI
     Preparation of naphththalene derivatives which inhibit the cytokine or
     biological activity of macrophage migration inhibitory factor (MIF)
     Morand, Eric Francis; Iskander, Magdy Naguib
ΙN
PΑ
     Cortical Pty. Ltd., Australia
SO
     PCT Int. Appl., 157 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 2
     PATENT NO.
                         KIND
                                 DATE
                                             APPLICATION NO.
                                                                     DATE
PΙ
     WO 2003104178
                          Α1
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                                             WO 2003-AU716
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
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     CA 2487866
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                                                                     20030606
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                                             EP 2003-724672
                                                                     20030606
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             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
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                                             IN 2004-KN1844
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                                             US 2005-517240
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PRAI AU 2002-2833
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                                 20020607
     AU 2002-2834
                                 20020607
                          Α
     WO 2003-AU716
                          W
                                 20030606
OS
     MARPAT 140:27670
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$$R^{5}$$
 $R^{4}$ 
 $R^{3}$ 
 $R^{2}$ 
 $R^{6}$ 
 $R^{7}$ 
 $R^{8}$ 

Ι

GΙ

AB Title compds. I [Y = O, NR9, SOq; R1 = H, alkyl, alkylhalo, alkylalkoxy, etc.; ] are prepared For instance, 2,3-dimethoxynaphthalene (preparation given) is acetylated (PhNO2, AcCl, AlCl3) and converted to 6,7-dimethoxy-2- naphthoic acid (water, NaOH, 85°, 60 min). Example compds. are inhibitors of the cytokine or biol. activity of macrophage migration inhibitory factor (MIF). I are useful for the treatment of Lyme disease, connective tissue diseases, etc.

IT 634197-33-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of naphththalene derivs. which inhibit the cytokine or biol. activity of macrophage migration inhibitory factor (MIF))

RN 634197-33-4 CAPLUS

CN Butanedioic acid, [(4-methoxy-2-methylphenyl)methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:847388 CAPLUS <u>Full-text</u>

DN 140:37671

TI 'Molecular Model of the  $\alpha \text{IIb}\beta 3$  Integrin

AU Feuston, Bradley P.; Culberson, J. Christopher; Hartman, George D.

CS Department of Molecular Systems, Merck Research Laboratories, West Point, PA, 19486, USA

SO Journal of Medicinal Chemistry (2003), 46(25), 5316-5325 CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

AB A mol. model of the  $\alpha IIb\beta 3$  integrin has been developed utilizing (i) the crystal structure of  $\alpha v \beta 3$ , (ii) homol. model of the  $\alpha IIb$  subdomain, and (iii) the docking of  $\alpha IIb\beta 3/\alpha v\beta 3$  dual and selective inhibitors into the putative binding sites of  $\alpha IIb\beta 3$  and  $\alpha v\beta 3$ . Since the binding sites of these integrins are located at the interface between the two heads of the individual subunits, only the  $\alpha IIb \beta 3$  head region is modeled. The 3D conformations of two loops in  $lpha ext{IIb}$ , whose residues have been implicated in non-peptide ligand binding, could not be determined from homol. with  $\alpha v$  alone. Mutagenesis data and the modeling of small ligand binding contributed to the rational design of these loop conformations. The final energy minimized loop conformations exhibit permissible  $\phi/\psi$  angles and contribute to a binding site model of  $\alpha IIb\beta 3$  that is consistent with both the known mutagenesis studies and inhouse structureactivity relationships. The charged residues  $\alpha \text{IIb:E117}$  and  $\beta 3:R214$  are found to dominate the ligand-protein binding interaction. The previously identified "exosite" is also identified as a hydrogen bond, hydrophobic or  $\pi\text{-}\pi$ interaction with Y190, similar to the recently proposed binding model of  $\alpha v \beta 3$ . ΙT 637032-80-5

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(building of mol. model of  $\alpha IIb\beta 3$  integrin using a known crystal structure, homol. modeling, and selective inhibitor interaction)

RN 637032-80-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(trifluoromethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:705668 CAPLUS Full-text

DN 140:2336

TI A Humanized Aldolase Antibody for Selective Chemotherapy and Adaptor Immunotherapy

AU Rader, Christoph; Turner, James M.; Heine, Andreas; Shabat, Doron; Sinha, Subhash C.; Wilson, Ian A.; Lerner, Richard A.; Barbas, Carlos F.

CS The Skaggs Institute for Chemical Biology and the Department of Molecular Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA

SO Journal of Molecular Biology (2003), 332(4), 889-899 CODEN: JMOBAK; ISSN: 0022-2836

PB Elsevier

DT Journal

LA English

AB Mouse monoclonal antibody 38C2 is the prototype of a new class of catalytic antibodies that were generated by reactive immunization. Through a reactive lysine, 38C2 catalyzes aldol and retro-aldol reactions using the enamine mechanism of natural aldolases. In addition to its remarkable versatility and efficacy in synthetic organic chemical, 38C2 has been used for the selective activation of prodrugs in vitro and in vivo and thereby emerged as a promising tool for selective chemotherapy. Adding another application with relevance for cancer therapy, designated adaptor immunotherapy, we have recently shown that 38C2 can be chemical programmed to target tumors by formation of a covalent bond of defined stoichiometry with a  $\beta$ -diketone derivative of an integrin  $\alpha v \beta 3$  targeting RGD peptidomimetic. However, a major limitation for the transition from preclin. to clin. evaluation is the human anti-mouse antibody immune response that mouse 38C2 is likely to elicit in a majority of patients after single administration. Here, we report the humanization of mouse 38C2 based on rational design guided by mol. modeling. In essence, the catalytic center of mouse 38C2, which encompasses a deep hydrophobic pocket with a reactive lysine residue at the bottom, was grafted into a human antibody framework. Humanized 38C2 IgG1 was found to bind to  $\beta$ -diketone haptens with conserved affinities and revealed strong catalytic activity with identical kcat and slightly higher KM values compared to the parental mouse antibody. Furthermore, humanized 38C2 IgG1 revealed efficiency in prodrug activation and chemical programming comparable to the parental mouse antibody.

IT 518315-49-6

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)

(humanized aldolase antibody for selective chemotherapy and adaptor immunotherapy)

RN 518315-49-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-[19-[[4-(3,5-dioxohexyl)phenyl]amino]-15,19-dioxo-4,7,10-trioxa-14-azanonadec-1-yl]-2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

Me-C-CH<sub>2</sub>-C-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>

NH-C-(CH<sub>2</sub>)<sub>3</sub>-C-NH-(CH<sub>2</sub>)<sub>3</sub>-O-CH<sub>2</sub>-

PAGE 1-A

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
L11
     ANSWER 14 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ΑN
     2003:570731 CAPLUS Full-text
DN
     139:138717
     Catalytic antibody targeting compounds
TI
ΙN
     Barbas, Carlos F.; Rader, Christoph; Sinha, Subhash C.; Lerner, Richard
PΑ
     The Scripps Research Institute, USA
     PCT Int. Appl., 112 pp.
SO
     CODEN: PIXXD2
DT.
     Patent
     English
LA
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                    DATE
PΙ
     WO 2003059251
                          Α2
                                20030724
                                            WO 2002-US33991
                                                                    20021022
     WO 2003059251
                          A3
                                20040219
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2464472
                          Α1
                                20030724
                                            CA 2002-2464472
                                                                    20021022
     AU 2002365182
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                                20030730
                                            AU 2002-365182
                                                                    20021022
     US 2003175921
                          A1
                                20030918
                                            US 2002-278364
                                                                    20021022
     EP 1443963
                          Α2
                                20040811
                                            EP 2002-804108.
                                                                    20021022
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     CN 1606454
                                20050413
                                            CN 2002-825631
                          Α .
                                                                    20021022
     JP 2005514430
                          Т
                                20050519
                                             JP 2003-559416
                                                                    20021022
     US 2003190676
                          Α1
                                20031009
                                            US 2003-420373
                                                                   . 20030421
PRAI US 2001-344614P
                          Ρ
                                20011022
     US 2002-412455P
                                20020919
                          Ρ
     US 2002-278364
                          A1
                                20021022
     WO 2002-US33991
                          W
                                20021022
AΒ
     The present invention provides antibody targeting compds. in which the
     specificity of the antibody has been reprogrammed by covalently or
     noncovalently linking a targeting agent to the combining site of an antibody.
     By this approach, the covalently modified antibody takes on the binding
     specificity of the targeting agent. The compound may have biol. activity
     provided by the targeting agent or by a sep. biol. agent. Various uses of the
     invention compds. are provided.
IT
     205677-92-5 518315-47-4
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (catalytic antibody targeting compds.)
RN
     205677-92-5 CAPLUS
     1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-
     pyridinylamino)propoxy] - (9CI) (CA INDEX NAME)
```

RN 518315-47-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L11 ANSWER 15 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:373179 CAPLUS Full-text

DN 139:101016

TI Convenient Synthesis of 2-Benzazepines via Radical Cyclization

AU Kamimura, Akio; Taguchi, Yohei; Omata, Yoji; Hagihara, Masahiko

CS Department of Applied Chemistry Faculty of Engineering, Yamaguchi University, Ube, 755-8611, Japan

SO Journal of Organic Chemistry (2003), 68(12), 4996-4998 CODEN: JOCEAH; ISSN: 0022-3263

PB American Chemical Society

DT Journal

LA English

OS CASREACT 139:101016

GΙ

$$\begin{array}{c}
R \\
N \\
R^2
\end{array}$$

$$\begin{array}{c|c} R & O & R^2 \\ \hline \\ Br & R^1 & CH_2 \end{array}$$

AB Benzazepines I (R = H, MeO; R1 = F3C, Ph, Pr; R2 = Me, MeO2CCH2, EtO2CCH2) were prepared via 7-endo radical cyclization of N-o-bromobenzylitaconamides or N-o-bromobenzylmethacrylamides II, which were prepared in two steps from com. available benzaldehydes, amines, and  $\alpha,\beta$ -unsatd. acids.

IT 558484-04-1P 558484-07-4P 558484-10-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of benzazepines via reductive amination of bromobenzaldehydes, propencylation of benzylamines, and radical cyclization of (bromobenzyl) propenamides)

RN 558484-04-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-2-(2,2,2-trifluoroethyl)-, ethyl ester (9CI) (CA INDEX NAME)

EtO-
$$C$$
- $CH_2$ 
OMe
$$F_3C-CH_2$$

RN 558484-07-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-2-(phenylmethyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 558484-10-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-butyl-2,3,4,5-tetrahydro-8-methoxy-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 16 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:368166 CAPLUS Full-text

DN 138:400106

TI Chemically programmed monoclonal antibodies for cancer therapy: Adaptor immunotherapy based on a covalent antibody catalyst

AU Rader, Christoph; Sinha, Subhash C.; Popkov, Mikhail; Lerner, Richard A.; Barbas, Carlos F., III

CS Department of Molecular Biology and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA

SO Proceedings of the National Academy of Sciences of the United States of America (2003), 100(9), 5396-5400 CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

Proposing that a blend of the chemical diversity of small synthetic mols. with AΒ the immunol. characteristics of the antibody mol. will lead to therapeutic agents with superior properties, the authors here present a device that equips small synthetic mols. with both effector function and long serum half-life of a generic antibody mol. As a prototype, the authors developed a targeting device that is based on the formation of a covalent bond of defined stoichiometry between a 1,3-diketone derivative of an integrin  $\alpha v\beta 3$  and  $\alpha v\beta 5$ targeting Arg-Gly-Asp peptidomimetic and the reactive lysine of aldolase antibody 38C2. The resulting complex was shown to (i) spontaneously assemble in vitro and in vivo, (ii) selectively retarget antibody 38C2 to the surface of cells expressing integrins  $\alpha v \beta 3$  and  $\alpha v \beta 5$ , (iii) dramatically increase the circulatory half-life of the Arg-Gly-Asp peptidomimetic, and (iv) effectively reduce tumor growth in animal models of human Kaposi's sarcoma and colon cancer. This immunotherapeutic has the potential to target a variety of human cancers, acting on both the vasculature that supports tumor growth as well as the tumor cells themselves. Further, by use of a generic antibody mol. that forms a covalent bond with a 1,3-diketone functionality, essentially any compound can be turned into an immunotherapeutic agent thereby not only increasing the diversity space that can be accessed but also multiplying the therapeutic effect.

IT 518315-49-6, SCS 873

RL: BSU (Biological study, unclassified); BIOL (Biological study) (SCS 873; adaptor immunotherapy based on a covalent antibody catalyst)

RN 518315-49-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-[19-[[4-(3,5-dioxohexyl)phenyl]amino]15,19-dioxo-4,7,10-trioxa-14-azanonadec-1-yl]-2,3,4,5-tetrahydro-3-oxo-8[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

PAGE 1- $\mathring{A}$ Me— $\mathring{C}$ — $\mathring{C}$ + $\mathring{C$ 

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 17 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ΑN
     2003:334841 CAPLUS Full-text
DN
     138:358451
ΤI
     Integrin targeting compounds
IN
     Barbas, Carlos F.; Rader, Christoph; Sinha, Subhash C.
PA
     The Scripps Research Institute, USA
SO
     PCT Int. Appl., 68 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                    DATE
                         ____
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                                            -----
PΙ
     WO 2003034995
                          A2
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                                            WO 2002-US33866
                                                                    20021022
     WO 2003034995
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2464271
                         · A1
                                20030501
                                           CA 2002-2464271
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     AU 2002337954
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                                                                    20021022
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                          A1
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                                            US 2002-278539
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     EP 1446418
                          A2
                                20040818
                                            EP 2002-773859
                                                                    20021022
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             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     CN 1606566
                          Α
                                20050413
                                            CN 2002-825588
                                                                    20021022
     JP 2005532252
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                                20051027
                                            JP 2003-537564
                                                                    20021022
PRAI US 2001-343799P
                          Ρ
                                20011022
     US 2002-412519P
                          Р
                                20020919
     WO 2002-US33866
                          W
                                20021022
     The present invention is directed to integrin targeting compds. comprising an
     integrin targeting component linked to a functional component such as a
     therapeutic agent or antibody. Structures of various integrin targeting
     compds., e.g. a RGD peptidomimetic, are provided. Also, methods of delivering
     a functional component to integrin associated with cells or tissue of an
     individual using the integrin targeting compds., as well as methods of
     treating or preventing a disease or condition in an individual wherein the
     disease or condition involves an integrin using the integrin targeting compds.
     are described. For example, a diketone version of a RGD peptidomimetic
     specific for human integrin (a binding affinity for \alpha V\beta 3 = 0.9 nM and for \alpha V\beta 5
     = 0.6 nM), designated SCS-873, was prepared and used for synthesis of the
     paclitaxel derivative with better soluble paclitaxel-SCS-873.
ΙT
     518315-53-2P, Etoposide-SCS 873
     RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (preparation of integrin targeting compds. containing therapeutic agents or
        antibody)
RN
     518315-53-2 CAPLUS
CN
     1H-2-Benzazepine-4-acetic acid, 2-[26-[4-[(5R,5aR,8aR,9S)-9-[[4,6-0-(1R)-
     ethylidene-\beta-D-glucopyranosyl]oxy]-5,5a,6,8,8a,9-hexahydro-6-
     oxofuro[3', 4':6, 7] naphtho[2, 3-d]-1, 3-dioxol-5-yl]-2, 6-dimethoxyphenoxy]-
     22,25-dimethyl-15,17,21,26-tetraoxo-4,7,10,20-tetraoxa-14,22,25-
     triazahexacos-1-yl]-2,3,4,5-tetrahydro-3-oxo-8-[3-(2-
     pyridinylamino)propoxy] - (9CI) (CA INDEX NAME)
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L11

Absolute stereochemistry.

## PAGE 1-B

H

PAGE 2-C

IT 205677-92-5 518315-47-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of integrin targeting compds. containing therapeutic agents or antibody)

RN 205677-92-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

RN 518315-47-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 518315-49-6F, SCS 873.518329-32-3P, SCS 1655
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of integrin targeting compds. containing therapeutic agents or antibody)

RN 518315-49-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-[19-[[4-(3,5-dioxohexyl)phenyl]amino]-15,19-dioxo-4,7,10-trioxa-14-azanonadec-1-yl]-2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 518329-32-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,2'-[21-[5-[[4-(3,5-dioxohexyl)phenyl]amino]-1,5-dioxopentyl]-15,27-dioxo-4,7,10,32,35,38-hexaoxa-14,21,28-triazahentetracontane-1,41-diyl]bis[2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-C

ΙT 518315-51-0P RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (preparation of integrin targeting compds. containing therapeutic agents or antibody) 518315-51-0 CAPLUS RN 1H-2-Benzazepine-4-acetic acid, 2-[22-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-CN  $\alpha$ -L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-15,19,22-trioxo-4,7,10,20-tetraoxa-14azadocos-1-yl]-2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

RN 518315-49-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-[19-[[4-(3,5-dioxohexyl)phenyl]amino]-15,19-dioxo-4,7,10-trioxa-14-azanonadec-1-yl]-2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-(9CI) (CA INDEX NAME)

PAGE 1-A

RN 518315-50-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-[20-[[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl]oxy]carbonyl]-15,18,23-trioxo-21,23-diphenyl-4,7,10-trioxa-14,22-diazatricos-1-yl]-2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 518315-52-1 CAPLUS

CN  $1H-2-Benzazepine-4-acetic acid, 2-[22-[(2S,4S)-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-4-[[2,3,6-trideoxy-3-(2,3-dihydro-1H-pyrrol-1-yl)-<math>\alpha$ -L-lyxo-hexopyranosyl]oxy]-2-naphthacenyl]-15,19,22-trioxo-4,7,10,20-tetraoxa-14-azadocos-1-yl]-2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

PAGE 1-B

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ANSWER 18 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
     2003:319691 CAPLUS Full-text
ΑN
DN
     138:326535
TI
    Methods for preventing and treating bone loss in postmenopausal or
     ovariectomized women with steroid compounds
     Di Salle, Enrico; Massimini, Giorgio; Lowery, Colin; Goss, Paul Edward
ΙN
PΑ
     Pharmacia Italia S.p.A., Italy; Pharmacia & Upjohn Company
SO
     PCT Int. Appl., 16 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 1
     PATENT NO.
                         KIND
                                 DATE
                                             APPLICATION NO.
                                                                     DATE
PΙ
     WO 2003032961
                          A2
                                 20030424
                                             WO 2002-EP11123
                                                                    .20020930
     WO 2003032961
                          А3
                                 20030904
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             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KĠ, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2463142
                          Α1
                                 20030424
                                             CA 2002-2463142
                                                                     20020930
     AU 2002333895
                          A1
                                 20030428
                                             AU 2002-333895
                                                                    20020930
     EP 1435967
                          A2
                                 20040714
                                             EP 2002-801313
                                                                    20020930
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     BR 2002013162
                          Α
                                20040914
                                             BR 2002-13162
                                                                     20020930
     JP 2005508958
                          ·T
                                 20050407
                                             JP 2003-535765
                                                                     20020930
     CN 1713915
                          A
                                 20051228
                                             CN 2002-820116
                                                                     20020930
     NZ 532064
                          Α
                                 20060428
                                             NZ 2002-532064
                                                                     20020930
     ZA 2004002734
                                             ZA 2004-2734
                          Α
                                 20050113
                                                                     20040407
PRAI US 2001-328209P
                          Ρ
                                 20011010
     WO 2002-EP11123
                          W
                                20020930
AΒ
     A method of preventing and treating abnormal metabolic bone disorders in a
     postmenopausal or oophorectomized woman is disclosed, which comprises
     administering an effective amount of exemestane or 17-hydro-exemestane, alone
     or in combination with addnl. therapeutic agents. Further methods for
     treating bone disorders are claimed, comprising the administration of
     exemestane or 17-hydro-exemestane simultaneously, sep. or sequentially with an
     addnl. therapeutic agent selected from the group consisting of a selective
     estrogen receptor modulator, an \alpha v \beta 3 inhibitor or antagonist, a vitamin D or
     vitamin D derivative, sodium fluoride, a COX-2 inhibitor and a biophosphonate
     compound, or a mixture thereof.
ΙT
     205678-31-5, SB-273005
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (methods and compds. for preventing and treating bone loss in
        postmenopausal or ovariectomized women with steroid compds.
        administered in conjunction with an \alpha v \beta 3 inhibitor or
        antagonist)
RN
     205678-31-5 CAPLUS
```

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

```
ANSWER 19 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
     2002:868905 CAPLUS Full-text
AN
DN
     137:370076
TΙ
     Preparation of naphthyridinylethoxybenzazepinones and related compounds as
     αv integrin receptor antagonists
     Meissner, Robert S.; Coleman, Paul J.; Duggan, Mark E.; Hartman, George
ΙN
     D.; Hutchinson, John H.; Wang, Jiabing
     Merck & Co., Inc., USA
PA
SO
     PCT Int. Appl., 55 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                             APPLICATION NO.
                                                                    DATE
                         ____
PΙ
     WO 2002090325
                          A2
                                             WO 2002-US13457
                                20021114
                                                                    20020429
     WO 2002090325
                          А3
                                20030227
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
             UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2445679
                          Α1
                                20021114
                                             CA 2002-2445679
                                                                    20020429
     AU 2002256387
                          Α1
                                             AU 2002-256387
                                20021118
                                                                    20020429
     EP 1387688
                          A2
                                20040211
                                             EP 2002-725848
                                                                    20020429
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004528373
                                20040916
                                             JP 2002-587405
                          Т
                                                                    20020429
     US 2004142919
                          A1
                                20040722
                                             US 2003-475697
                                                                    20031021
     US 7109191
                          B2
                                20060919
PRAI US 2001-288578P
                          Р
                                20010503
     WO 2002-US13457
                          W .
                                20020429
OS
     MARPAT 137:370076
GI
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$$\begin{array}{c|c} x & & \\ \hline & & \\$$

Title compds. [I; X = (substituted) tetrahydronaphthyridinyl, pyridoazepinyl, aminopyridinyl; R1 = H, alkyl], were prepared as antagonists of the integrin receptors  $\alpha v\beta 3$  and  $\alpha v\beta 5$  and are therefore useful for inhibiting bone resorption, treating and/or preventing osteoporosis, and inhibiting vascular restenosis, diabetic retinopathy, macular degeneration, angiogenesis, atherosclerosis, inflammatory arthritis, cancer, and metastatic tumor growth (no data). Thus, 5,6,7,8-tetrahydro-1,8-naphthyridin-2-ylethanol, Me (4S)-3-oxo-8-hydroxy-2-(2,2,2-trifluoroethyl)-2,3,4,5-tetrahydro-1H-2- benzazepin-4-

acetate, Ph3P, and di-Et azodicarboxylate were stirred in THF at 0° to room temperature to give the ether coupling product, which was saponified with aqueous NaOH in dioxane to give (4S)-3-oxo-8-[2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethoxy]-2-(2,2,2-trifluoroethyl)-2,3,4,5-tetrahydro-1H-benzazepin-4-acetic acid.

IT 475204-25-2P 475204-26-3P 475204-27-4P 475204-28-5P 475204-29-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of naphthyridinylethoxybenzazepinones and related compds. as  $\alpha v$  integrin receptor antagonists)

RN 475204-25-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[2-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)ethoxy]-2-(2,2,2-trifluoroethyl)-, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 475204-26-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[2-(1,5,6,7-tetrahydro-7-methyl-1,8-naphthyridin-2-yl)ethoxy]-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 475204-27-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[2-(5,6,7,8-tetrahydro-1H-pyrido[2,3-b]azepin-2-yl)ethoxy]-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 475204-28-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[2-(2',3'-dihydrospiro[cyclopropane-1,4'(1'H)-[1,8]naphthyridin]-7'-yl)ethoxy]-2,3,4,5-tetrahydro-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 475204-29-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[2-[3-cyclopropyl-6-(methylamino)-2-pyridinyl]ethoxy]-2,3,4,5-tetrahydro-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 475204-30-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of naphthyridinylethoxybenzazepinones and related  $\ensuremath{\mathsf{I}}$ 

compds. as  $\alpha v$  integrin receptor antagonists)

RN 475204-30-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[2-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)ethoxy]-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 205677-04-9

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of naphthyridinylethoxybenzazepinones and related compds. as  $\alpha v$  integrin receptor antagonists)

RN 205677-04-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L11 ANSWER 20 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:844382 CAPLUS Full-text

DN 138:66643

TI Binding Model for Nonpeptide Antagonists of  $\alpha \dot{\nu} \beta 3$  Integrin

AU Feuston, Bradley P.; Culberson, J. Chris; Duggan, Mark E.; Hartman, George D.; Leu, Chih-Tai; Rodan, Sevgi B.

CS Departments of Molecular Systems Medicinal Chemistry and Bone Biology Osteoporosis Research, Merck Research Laboratories, West Point, PA, 19486, USA

SO Journal of Medicinal Chemistry (2002), 45(26), 5640-5648 CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

AB A binding model for nonpeptide antagonists of integrin  $\alpha v \beta 3$  has been developed through docking analyses utilizing the MMFFs force field and the recently published crystal structure, 1JV2. Results of this docking study have led to the identification of a novel binding model for selective antagonists of  $\alpha v \beta 3$ over  $\alpha \text{IIb}\beta 3$  integrins. Four different chemical classes are shown to bind in a similar fashion providing a measure of confidence in the proposed model. All  $\alpha v\beta 3$  and  $\alpha IIb\beta 3$  antagonists have a basic nitrogen separated some distance from a carboxylic acid to mimic RGD. For the  $\alpha v\beta 3$  antagonists under present consideration, these charged ends are separated by twelve bonds. The basic nitrogen of the active  $\alpha v\beta 3$  ligands are shown to interact with D150 of  $\alpha v$  and the ligands' carboxylic acid interact with R214 of  $\beta 3$  while adopting an extended conformation with minimal protein induced internal strain. In addition, an energetically favorable interaction is found with all of the active  $\alpha v\beta 3$  mols. with Y178 of  $\alpha v$  when docked to the crystallog. determined structure. This novel interaction may be characterized as  $\pi\text{-}\pi$  stacking for the most active of the  $\alpha v \beta 3$  selective antagonists. The proposed model is consistent with observed activity as well as mutagenicity and photoaffinity crosslinking studies of the  $\alpha v\beta 3$  integrin.

IT 205678-31-5

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(binding model for nonpeptide antagonists of  $\alpha v \beta 3$  integrin)

RN 205678-31-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
L11
     ANSWER 21 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
     2002:813921 CAPLUS Full-text
AN
DN
     137:304827
TI
     Method of inhibiting adhesion formation
ΙN
     Willette, Robert N.
PΑ
     Smithkline Beecham Corporation, USA
SO
     PCT Int. Appl., 22 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                    DATE
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                                            ______
PΙ
     WO 2002083125
                          A1
                                20021024
                                          . WO 2002-US11285
                                                                    20020410
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
             US, UZ, VN, YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2443734
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                                20021028
                                            AU 2002-305164
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     EP 1385504
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                                            EP 2002-733968
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             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     HU 200303725
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                                            CN 2002-809787
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     JP 2004525959
                          Τ
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                                            JP 2002-580929
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     NZ 528577
                          Α
                                20050128
                                            NZ 2002-528577
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     ZA 2003007621
                          Α
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                                            ZA 2003-7621
                                                                    20030930
     BG 108217
                          Α
                                20041230
                                            BG 2003-108217
                                                                    20031001
     NO 2003004513
                          Α
                                20031204
                                            NO 2003-4513
                                                                    20031008
     US 2004142918
                          Α1
                                20040722
                                            US 2003-474540
                                                                    20031009
     MX 2003PA09344
                          Α
                                20040212
                                            MX 2003-PA9344
                                                                    20031010
     IN 2003DN01702
                          Α
                                20051014
                                            IN 2003-DN1702
                                                                    20031017
     US 2007149505
                          Α1
                                20070628
                                            US 2007-676359
                                                                    20070219
PRAI US 2001-282693P
                          Ρ
                                20010410
     WO 2002-US11285
                          W
                                20020410
     US 2003-474540
                          Α1
                                20031009
AB
     The invention discloses the use of a vitronectin receptor antagonist to
     inhibit adhesion formation.
ΙT
     205678-26-8 205678-31-5
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (method of inhibiting adhesion formation)
RN
     205678-26-8 CAPLUS
CN
     1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-6)]
     pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)-, (4S)- (CA INDEX NAME)
```

Absolute stereochemistry. Rotation (-).

RN 205678-31-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methýlamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 22 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:520405 CAPLUS Full-text

DN 138:117608

TI Rapid inhibition of thyroxine-induced bone resorption in the rat by an orally active vitronectin receptor antagonist

AU Hoffman, Sandra J.; Vasko-Moser, Janice; Miller, William H.; Lark, Michael W.; Gowen, Maxine; Stroup, George

CS Departments of Musculoskeletal Diseases, GlaxoSmithKline, King of Prussia, PA, USA

SO Journal of Pharmacology and Experimental Therapeutics (2002), 302(1), 205-211

CODEN: JPETAB; ISSN: 0022-3565

PB American Society for Pharmacology and Experimental Therapeutics

DT Journal

LA English

AΒ An excess of thyroid hormone results in increased bone turnover and loss of bone mass in humans. Exogenous administration of thyroid hormone to rats has served as a model of human hyperthyroidism in which antiresorptive therapies have been tested. We have further refined this model of thyroxine (T4)induced turnover in the rat. Daily administration of T4 to aged rats for as short as 1 wk resulted in elevated bone resorption determined by significantly higher urinary deoxypyridinoline (Dpd) compared with vehicle controls or animals receiving T4 plus estradiol. Three weeks of daily administration of T4 led to significantly lower bone mineral d. compared with untreated controls or animals receiving T4 plus estradiol. In a follow-up study, a depot formulation of T4 caused an increase in Dpd identical to that achieved with a bolus dose. SB-273005 [(4S)-2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2pyridinyl]ethoxy]-3-oxo-2- (2,2,2-trifluoroethyl)-1H-2-benzazepine-4-acetic acid] a potent antagonist of the integrins  $\alpha v\beta 3$  and  $\alpha v\beta 5$  , has been shown previously to inhibit bone resorption in cultures of human osteoclasts and to protect bone in ovariectomized rats. The effect of SB-273005 by oral administration was evaluated in this thyroxine-induced turnover model. Dosedependent inhibition of resorption was seen with SB-273005 after 7 days of dosing using Dpd as a measure of bone resorption. In summary, it has been demonstrated that the antiresorptive activity of a vitronectin receptor antagonist can be measured after only 7 days of treatment in this refined rat model of thyroxine-induced bone turnover. These data suggest that SB-273005 may be useful for the treatment of metabolic bone diseases, including those resulting from hyperthyroidism.

IT 205678-31-5, SB 273005

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(orally active vitronectin receptor antagonist inhibition of thyroxine-induced bone resorption)

RN 205678-31-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 23 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:128172 CAPLUS Full-text

DN 135:132013

Disease-modifying activity of SB 273005, an orally active, nonpeptide  $\alpha v \beta 3$  (vitronectin receptor) antagonist, in rat adjuvant-induced arthritis

AU Badger, Alison M.; Blake, Simon; Kapadia, Rasesh; Sarkar, Susanta; Levin, Joshua; Swift, Barbara A.; Hoffman, Sandy J.; Stroup, George B.; Miller, William H.; Gowen, Maxine; Lark, Michael W.

CS SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA

SO Arthritis & Rheumatism (2001), 44(1), 128-137 CODEN: ARHEAW; ISSN: 0004-3591

PB Wiley-Liss, Inc.

DT Journal

LA English

Objective. To evaluate the effects of SB 273005, a potent, orally active AB nonpeptide antagonist of the integrin  $\alpha v\beta 3$  vitronectin receptor, on joint integrity in rats with adjuvant-induced arthritis (AIA). Methods. Male Lewis rats with AIA were orally dosed either prophylactically (days 0-20) or therapeutically (days 10-20) with SB 273005. Efficacy was determined by measurement of paw inflammation, assessment of bone mineral d. using dualenergy x-ray absorptiometry (DEXA), magnetic resonance imaging (MRI), and histol. evaluation. Results. SB 273005 is a potent antagonist of the closely related integrins,  $\alpha v \beta 3$  (Ki = 1.2 nM) and  $\alpha v \beta 5$  (Ki = 0.3 nM). When SB 273005 was administered prophylactically to AIA rats twice per day, it inhibited paw edema at doses of 10, 30, and 60 mg/kg, by 40%, 50%, and 52%, resp. Therapeutic administration twice daily was also effective, and a reduction in paw edema was observed at 30 mg/kg and 60 mg/kg of the antagonist (by 36% and 48%, resp.). SB 273005 was also effective when administered once per day, both prophylactically and therapeutically. Significant improvement in joint integrity in treated rats was shown using DEXA and MRI analyses. These findings were confirmed histol., and significant protection of bone, cartilage, and soft tissue was observed within the joint. Conclusion. Symptoms of AIA in rats were significantly reduced by either prophylactic or therapeutic treatment with the  $\alpha v\beta 3$  antagonist, SB 273005. Measurements of paw inflammation and of bone, cartilage, and soft tissue structure indicated that this compound exerts a protective effect on joint integrity and thus appears to have disease-modifying properties.

IT: 205678-31-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(SB 273005 disease-modifying activity in rats with adjuvant-induced arthritis)  $\cdot$ 

RN 205678-31-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 24 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
L11
AN
     2001:115149 CAPLUS Full-text
DN
     134:157565
TI
     Vitronectin receptor antagonists useful for the treatment of strokes
ΙN
     Barone, Frank C.; Yue, Tian-Li
PΑ
     SmithKline Beecham Corporation, USA
SO
     PCT Int. Appl., 21 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                    DATE
                         ____
PI
     WO 2001010867
                          Α1
                                20010215
                                            WO 2000-US21433
                                                                    20000804
             AE, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CZ, DZ, EE, GE, GH, GM,
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             MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ, UA,
             US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1208101
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                                20020529 EP 2000-952558
                                                                    20000804
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             IE, SI, LT, LV, FI, RO, MK, CY, AL
     JP '2003506452
                                20030218
                          Т
                                            JP 2001-515676
                                                                    20000804
PRAI US 1999-147567P
                          Ρ
                                19990806
     WO 2000-US21433
                          W
                                20000804
OS.
     MARPAT 134:157565
AΒ
     This invention relates to the use of a vitronectin receptor antagonist to
     treat stroke. The antagonist is a benzazepine ether.
ΙT
     205678-26-8 205678-26-8D, pharmaceutically acceptable
     salts 205678-31-5 205678-31-5D, pharmaceutically
     acceptable salts
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (vitronectin receptor antagonists useful for treatment of strokes)
RN
     205678-26-8 CAPLUS
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CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)-, (4S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205678-26-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)-, (4S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205678-31-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205678-31-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L11 ANSWER 25 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
- AN 2001:93796 CAPLUS Full-text
- DN 135:102507
- TI Antagonism of the osteoclast vitronectin receptor with an orally active nonpeptide inhibitor prevents cancellous bone loss in the ovariectomized rat
- AU Lark, Michael W.; Stroup, George B.; Dodds, Robert A.; Kapadia, Rasesh; Hoffman, Sandra J.; Hwang, Shing Mei; James, Ian E.; Lechowska, Beata; Liang, Xiaoguang; Rieman, David J.; Salyers, Kevin L.; Ward, Keith; Smith, Brian R.; Miller, William H.; Huffman, William F.; Gowen, Maxine
- CS Department of Bone and Cartilage Biology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, USA
- SO Journal of Bone and Mineral Research (2001), 16(2), 319-327 CODEN: JBMREJ; ISSN: 0884-0431
- PB American Society for Bone and Mineral Research
- DT Journal
- LA English
- An orally active, nonpeptide Arg-Gly-Asp (RGD) mimetic  $\alpha v \beta 3$  antagonist, (S)-3-AΒ 0xo-8-[2-[6-(methylamino)-pyridin-2-yl]-1-ethoxy]-2-(2,2, 2-trifluoroethyl)-2,3,4,5-tetrahydro-1H-2-benzazepine-4-acetic acid (compound 1), has been generated, which prevented net bone loss and inhibited cancellous bone turnover in vivo. The compound binds  $\alpha v \beta 3$  and the closely related integrin  $\alpha v \beta 5$  with low nanomolar affinity but binds only weakly to the related integrins  $\alpha IIb\beta 3$ , and  $\alpha 5\beta 1$ . Compound 1 inhibited  $\alpha v\beta 3$ -mediated cell adhesion with an IC50 = 3 nM. More importantly, the compound inhibited human osteoclast-mediated bone resorption in vitro with an IC50 = 11 nM. In vivo, compound 1 inhibited bone resorption in a dose-dependent fashion, in the acute thyroparathyroidectomized (TPTX) rat model of bone resorption with a circulating EC50 .apprx.20 µM. When dosed orally at 30 mg/kg twice a day (b.i.d.) in the chronic ovariectomy (OVX)-induced rat model of osteopenia, compound 1 also prevented bone loss. At doses ranging from 3 to 30 mg/kg b.i.d., compound 1 partially prevented the OVX-induced increase in urinary deoxypyridinoline. In addition, the compound prevented the OVX-induced reduction in cancellous bone volume (BV), trabecular number (Tb.N), and trabecular thickness (Tb.Th), as assessed by quant. microcomputerized tomog. ( $\mu CT$ ) and static histomorphometry. Furthermore, both the 10-mg/kg and 30mg/kg doses of compound prevented the OVX-induced increase in bone turnover, as measured by percent osteoid perimeter (%0.Pm). Together, these data indicate that the  $\alpha v \beta 3$  antagonist compound 1 inhibits OVX-induced bone loss. Mechanistically, compound 1 prevents bone loss in vivo by inhibiting osteoclast-mediated bone resorption, ultimately preventing cancellous bone turnover.
- IT 205678-31-5
  - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    - (osteoclast vitronectin receptor antagonism with orally active nonpeptide inhibitor prevents cancellous bone loss in ovariectomized rats)
- RN 205678-31-5 CAPLUS
- CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L11 ANSWER 26 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
- AN 1999:807528 CAPLUS Full-text
- DN 132:146616
- TI Discovery of Orally Active Nonpeptide Vitronectin Receptor Antagonists Based on a 2-Benzazepine Gly-Asp Mimetic
- AU Miller, William H.; Alberts, Doreen P.; Bhatnagar, Pradip K.; Bondinell, William E.; Callahan, James F.; Calvo, Raul R.; Cousins, Russell D.; Erhard, Karl F.; Heerding, Dirk A.; Keenan, Richard M.; Kwon, Chet; Manley, Peter J.; Newlander, Kenneth A.; Ross, Stephen T.; Samanen, James M.; Uzinskas, Irene N.; Venslavsky, Joseph W.; Yuan, Catherine C.-K.; Haltiwanger, R. Curtis; Gowen, Maxine; Hwang, Shing-Mei; James, Ian E.; Lark, Michael W.; Rieman, David J.; Stroup, George B.; Azzarano, Leonard M.; Salyers, Kevin L.; Smith, Brian R.; Ward, Keith W.; Johanson, Kyung O.; Huffman, William F.
- CS Research & Development Division, SmithKline Beecham Pharmaceuticals, Collegeville, PA, 19426-0989, USA
- SO Journal of Medicinal Chemistry (2000), 43(1), 22-26 CODEN: JMCMAR; ISSN: 0022-2623
- PB American Chemical Society
- DT Journal
- LA English
- AB A new series of small mol. RGD mimetics that are highly potent, orally active  $\alpha v\beta 3$  antagonists is described. Selected members of this series are potent inhibitors of bone resorption in vitro and in vivo and have activity in an animal model of osteoporosis.
- IT 258282-33-6

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(preparation of orally active nonpeptide vitronectin receptor antagonists based on a 2-benzazepine gly-asp mimetic)

- RN 258282-33-6 CAPLUS
- CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-3-oxo-8-[3-(2-pyridinylamino)propoxy]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 205678-16-6P 205678-26-8P 205678-27-9P 205678-31-5P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process) (preparation of orally active nonpeptide vitronectin receptor antagonists based on a 2-benzazepine gly-asp mimetic)

RN 205678-16-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

RN 205678-26-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)-, (4S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205678-27-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205678-31-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 205676-76-2P 205676-77-3P 205676-78-4P 205677-02-7P 205677-04-9P 205677-80-1P

205677-81-2P 205677-86-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of orally active nonpeptide vitronectin receptor antagonists based on a 2-benzazepine gly-asp mimetic)

RN 205676-76-2 CAPLUS

CN Butanedioic acid, [[2-[[[(1,1-dimethylethoxy)carbonyl](2,2,2-trifluoroethyl)amino]methyl]-4-methoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 205676-77-3 CAPLUS

CN Butanedioic acid, [[4-methoxy-2-[[(2,2,2-trifluoroethyl)amino]methyl]pheny l]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 205676-78-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester (9CI) (CA INDEX NAME)

MeO\_C\_CH<sub>2</sub>
OMe
$$F_3C_-CH_2$$

RN 205677-02-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205677-04-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205677-80-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-81-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)-(CA INDEX NAME)

Absolute stereochemistry.

RN 205677-86-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 27 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
     1999:231510 CAPLUS Full-text
ΑN
DN
     130:237491
TI
     Preparation of benzazepineacetic acid derivative as vitronectin receptor
     antagonist
     Miller, William H.
ΙN
PΑ
     Smithkline Beecham Corporation, USA
SO
     PCT Int. Appl., 35 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
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                                                                      DATE
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PRAI US 1997-59867P
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     WO 1998-US19987
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     US 2000-509184
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     US 2001-956682
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OS
     MARPAT 130:237491
GI
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AB The title compound I, a vitronectin receptor antagonist, was prepared IT 221305-62-0P

CO2H

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of benzazepineacetic acid derivative as vitronectin receptor antagonist)

Ι

RN 221305-62-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-methyl-2-pyridinyl)amino]propoxy]-3-o'xo-2-[[4-(trifluoromethyl)phenyl]methyl]-,

Absolute stereochemistry.

IT 205676-64-8P 205676-65-9P 205676-79-5P

205676-80-8P 205676-81-9P 205676-82-0P

221313-50-4P 221313-51-5P 221313-52-6P

221313-53-7F

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of benzazepineacetic acid derivative as vitronectin receptor antagonist)

RN 205676-64-8 CAPLUS

CN Butanedioic acid, [[2-[[bis[(1,1-dimethylethoxy)carbonyl]amino]methyl]-4-methoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 205676-65-9 CAPLUS

CN Butanedioic acid, [[2-(aminomethyl)-4-methoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 205676-79-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-, methyl ester, (4R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 205676-80-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-, methyl ester, (4S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205676-81-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-, methyl ester, (4R)- (9CL) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 205676-82-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 221313-50-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl](1-oxido-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 221313-51-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl](1-

oxido-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-2-[(2,3,4-trifluorophenyl)methyl]-, (4S)- (9CI) (CA INDEX NAME)

## Absolute stereochemistry.

RN 221313-52-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-2-[(2,3,4-trifluorophenyl)methyl]-, (4S)-(9CI) (CA INDEX NAME)

## Absolute stereochemistry.

RN 221313-53-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-[(2,3,4-trifluorophenyl)methyl]-, (4S)- (9CI) (CA INDEX NAME)

## Absolute stereochemistry.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 28 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ΑN
     1999:231502 CAPLUS Full-text
DN
     130:237490
ΤI
     Preparation of benzazepineacetic acid derivative as vitronectin receptor
     antagonist
     Miller, William H.
IN
     Smithkline Beecham Corporation, USA
PA
     PCT Int. Appl., 40 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
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AB The title compound I, a vitronectin receptor antagonist, was prepared in several steps.

IT 221305-62-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of benzazepineacetic acid derivative as vitronectin receptor antagonist)

RN 221305-62-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-methyl-2-pyridinyl)amino]propoxy]-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 205676-64-8P 205676-65-9P 205676-79-5P

205676-80-8P 205676-81-9P 205676-82-0P

205676-91-1P 205676-92-2P 205677-00-5P

221305-59-5P 221305-60-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of benzazepineacetic acid derivative as vitronectin receptor antagonist)

RN 205676-64-8 CAPLUS

CN Butanedioic acid, [[2-[[bis[(1,1-dimethylethoxy)carbonyl]amino]methyl]-4-methoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 205676-65-9 CAPLUS

CN Butanedioic acid, [[2-(aminomethyl)-4-methoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 205676-79-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-, methyl ester, (4R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 205676-80-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-, methyl ester, (4S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205676-81-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 205676-82-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205676-91-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[[4-(trifluoromethyl)phenyl]methoxy]-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205676-92-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester, (4S)- (9CI) (CA INDEX

Absolute stereochemistry. Rotation (-).

RN 205677-00-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 221305-59-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-methyl-1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 221305-60-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-methyl-2-pyridinyl)amino]propoxy]-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$_{\rm F3C}$$
  $_{\rm MeO}$   $_{\rm O}$   $_{\rm CH_2}$   $_{\rm S}$   $_{\rm MeO}$   $_{\rm O}$ 

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L11 ANSWER 29 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
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AN 1998:239115 CAPLUS Full-text

DN 128:294793

TI Preparation of benzodiazepines and dibenzo[a,d]cycloheptanes for stimulating bone formation

IN Drake, Fred H.

PA Smithkline Beecham Corporation, USA; Drake, Fred H.

SO PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND DATE	APPLICATION NO.	DATE
ΡI	WO 9815278 W: JP, US	A1 19980416	WO 1997-US18178	19971007
	EP 946180		FR, GB, GR, IE, IT, LU, EP 1997-945563	MC, NL, PT, SE 19971007
ד ע מם	JP 2001501951 US 2002032187	T 20010213 A1 20020314	JP 1998-517727 US 2001-956659	19971007 20010920
PRAI	US 1996-27764P WO 1997-US18178 US 1999-284055	P 19961007 W 19971007 B1 19990407	· · · · · · · · · · · · · · · · · · ·	
OS GI	US 2000-639347 MARPAT 128:294793	A1 20000816		

$$R^4$$
 $X - X \stackrel{R^3}{\underset{R^2}{\longrightarrow}} 0$ 
 $R^4$ 
 $R^2$ 
 $R^2$ 
 $R^3$ 
 $R^3$ 

AΒ The title compds. [I or II; X-X1 = NR1CH, N:C, CR1:C, etc.; R1 = H, C1-6alkyl, Ar-C1-6 alkyl; R2 = (CH2)nCO2R'; R3 = H, C1-6 alkyl, Ar-C0-6 alkyl, etc.; R4 = W-(Q')p(CR'2)qU(CR'2)s; R' = H, C1-6 alkyl, C3-7 cycloalkyl, etc.; Q' = NR5, S, CR5; U = NR6C(O), C(O)NR6, CH2CO, etc.; R5, R6 = H, C1-6 alkyl, etc.; W = (un) substituted pyridyl, piperidinyl, imidazolyl, etc.; n = 1-2; p =0-1; q = 0-3; s = 0-3], integrin binding compds. which cause the release of osteocalcin from osteoblasts, and are therefore useful for treating osteoporosis, hyperparathyroidism, Paget's disease, hypercalcemia of malignancy, osteolytic lesions produced by bone metastasis, or bone loss due to immobilization or sex hormone deficiency, were prepared and formulated. Thus, treatment of Me  $(\pm)$ -7-carboxy-4- methyl-3-oxo-2,3,4,5-tetrahydro-1H-1,4benzodiazepine-2-acetate with SOC12 followed by reaction of the resulting intermediate with 2-(aminomethyl)benzimidazole.2HCl in the presence of pyridine and Et3N in CH2Cl2, and hydrolysis of the acetate with 1.0 LiOH in THF/H2O afforded the title compound I [X = NH; X1 = CH; R2 = CH2COOH; R3 = Me; R4 = {[(2-benzimdazolyl)methyl]amino}carbonyl]. Prepared compds. I or II showed EC50 of < 1  $\mu M$  in the ROS 17/2.8 osteocalcin assay.

IT 205677-90-3P 205677-92-5P 205678-30-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of benzodiazepines and dibenzo[a,d]cycloheptanes for stimulating bone formation)

RN 205677-90-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2-phenylethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-92-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

RN 205678-30-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-2-(2-phenylethyl)-8-[3-(2-pyridinylamino)propoxy]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 205676-61-5P 205676-64-8P 205676-65-9P 205676-66-0P 205676-68-2P 205676-69-3P 205676-70-6P 205676-71-7P 205677-16-3P 205677-17-4P 205677-18-5P 205677-19-6P

205677-43-6P 205677-44-7P 205677-45-8P 205677-87-8P 205677-88-9P 205677-89-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of benzodiazepines and dibenzo[a,d]cycloheptanes for stimulating bone formation)

RN 205676-61-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205676-64-8 CAPLUS

CN Butanedioic acid, [[2-[[bis[(1,1-dimethylethoxy)carbonyl]amino]methyl]-4-methoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 205676-65-9 CAPLUS

CN Butanedioic acid, [[2-(aminomethyl)-4-methoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 205676-66-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205676-68-2 CAPLUS

CN Butanedioic acid, [[2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]methyl]-

4-methoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 205676-69-3 CAPLUS

CN Butanedioic acid, 2-[[4-methoxy-2-[(methylamino)methyl]phenyl]methyl]-, 1,4-dimethyl ester (CA INDEX NAME)

RN 205676-70-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-2-methyl-3-oxo-, methyl ester (CA INDEX NAME)

$$\begin{array}{c} \text{MeO-} \overset{\text{O}}{\text{C}} \text{CH}_2 \\ \text{O} & \text{N} \end{array} \begin{array}{c} \text{OMe} \\ \text{Me} \end{array}$$

RN 205676-71-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-2-methyl-3-oxo-, methyl ester (CA INDEX NAME)

RN 205677-16-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-2-(2-phenylethyl)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-17-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-2-(2-phenylethyl)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-18-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-19-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-, ethyl ester (9CI) (CA INDEX NAME)

RN 205677-43-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-8-[3-[[[(4-nitrophenyl)methoxy]carbonyl]amino]propoxy]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-44-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-(3-aminopropoxy)-2,3,4,5-tetrahydro-2-methyl-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-45-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]propoxy]-2,3,4,5-tetrahydro-2-methyl-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-87-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-2-(2-phenylethyl)-, methyl ester, (S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-88-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-2-(2-phenylethyl)-8-[3-(2-pyridinylamino)propoxy]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-89-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2-phenylethyl)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 30 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
AN
     1998:219717 CAPLUS Full-text
DN
     128:282853
     Oxotetrahydrobenzazepine compounds for vitronectin receptor antagonists
ΤI
ΙN
     Callahan, James Francis; Cousins, Russell Donovan; Keenan, Richard M.;
     Kwon, Chet; Miller, William Henry; Uzinkas, Irene Nijole
PΑ
     Smithkline Beecham Corp., USA
SO
     PCT Int. Appl., 129 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
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                                                                     DATE
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US 2002-320084 A1 20021216 CASREACT 128:282853; MARPAT 128:282853

OS GI

$$R^{2O}$$
 $NR^{1}$ 
 $CH_{2CO_{2}H}$ 
 $III$ 
 $R''' \rightarrow G$ 
 $III$ 
 $IV$ 

The title compds. I [Rl = R7, (un)substituted A-CO-4 alkyl, A-C2-4 alkenyl, A-C2-4 alkynyl, etc.; A = H, C3-6 cycloalkyl, Het or Ar; R7 = COR8, COCR'2R9, etc.; R8 = OR', NR'R'', NR'SO2R', etc.; R9 = OR', CN, COR', etc.; R2 = II, III, IV, etc.; R' = H, C1-6 alkyl, Ar-CO-6 alkyl, C3-6 cycloalkyl-CO-6 alkyl; R' = R', COR', CO2R'; R''' = H, C1-6 alkyl, Ar-CO-6 alkyl, etc.; W = (CHRg)aU(CHRg)b; U = CO, O, OCO, etc.; G = NRe, S, O; Rg = H, C1-6 alkyl, Het-CO-6 alkyl, etc.; Re = H, C1-6 alkyl, Ar-CO-6 alkyl, etc.; a, b = 0, 1, 2] or a pharmaceutically acceptable salt thereof, are prepared The compds. are useful in the treatment of osteoporosis, angiogenesis, tumor growth and metastasis, atherosclerosis, restenosis and inflammation. Thus, (±)-8-[3-(2-pyridylamino)-1-propyloxy]-3-oxo-2,3,4,5-tetrahydro-1H-2-benzazepin-4-acetic acid and its parenteral and oral dosage unit compns. were prepared

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(oxotetrahydrobenzazepine compds. for vitronectin receptor antagonists) 205677-90-3 CAPLUS

1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2-phenylethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN

CN

IT 205677-92-5P 205677-93-6P 205677-94-7P 205677-95-8P 205677-96-9P 205677-97-0P 205677-98-1P 205678-02-0P 205678-03-1P 205678-04-2P 205678-05-3P 205678-06-4P 205678-07-5P 205678-08-6P 205678-09-7P 205678-10-0P 205678-11-1P 205678-12-2P 205678-13-3P 205678-14-4P 205678-15-5P 205678-16-6P 205678-20-2P 205678-13-3P 205678-20-2P 205678-21-3P

205678-22-4P 205678-24-6P 205678-25-7P 205678-26-8P 205678-27-9P 205678-28-0P 205678-29-1P 205678-31-5P 205678-32-6P 205678-33-7P 205678-34-8P 205678-35-9P 205678-36-0P 205678-37-1P 205678-38-2P 205678-39-3P 205678-40-6P 205678-41-7P 205678-42-8P 205678-44-0P 205678-45-1P 205678-46-2P 205678-47-3P 205678-48-4P 205678-49-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(oxotetrahydrobenzazepine compds. for vitronectin receptor antagonists) 205677-92-5 CAPLUS

1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

RN 205677-93-6 CAPLUS

RN

CN

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4-amino-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-(9CI) (CA INDEX NAME)

RN 205677-94-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-methoxy-2-pyridinyl)amino]propoxy]-3-oxo- (9CI) (CA INDEX NAME)

RN 205677-95-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-3-oxo-8-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

RN 205677-96-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-(1H-imidazol-2-ylamino)propoxy]-3-oxo- (9CI) (CA INDEX NAME)

RN 205677-97-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]propoxy]- (9CI) (CA INDEX NAME)

RN 205677-98-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(6-amino-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-(9CI) (CA INDEX NAME)

RN 205677-99-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[2-(1H-benzimidazol-2-yl)ethoxy]-2,3,4,5-tetrahydro-3-oxo- (9CI) (CA INDEX NAME)

RN 205678-00-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-(1H-imidazo[4,5-b]pyridin-2-yl)ethoxy]-3-oxo- (9CI) (CA INDEX NAME)

RN 205678-01-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo- (9CI) (CA INDEX NAME)

RN 205678-02-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4-amino-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-2-methyl-3-oxo-(9CI) (CA INDEX NAME)

RN 205678-03-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyrimidinylamino)propoxy]- (9CI) (CA INDEX NAME)

RN 205678-04-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4-amino-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN. 205678-05-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4-amino-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205678-06-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl]-2-pyridinylamino]propoxy]-2,3,4,5-tetrahydro-3-oxo- (9CI) (CA INDEX NAME)

RN 205678-07-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl](1-oxido-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo- (9CI) (CA INDEX NAME)

RN 205678-08-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl]-2-pyridinylamino]propoxy]-2,3,4,5-tetrahydro-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

RN 205678-09-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

RN 205678-10-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-8-[3-(methyl-2-pyridinylamino)propoxy]-3-oxo- (9CI) (CA INDEX NAME)

RN 205678-11-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-2-(phenylmethyl)-

8-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

RN 205678-12-2 CAPLUS

CN 2H-2-Benzazepine-2,4-diacetic acid, 1,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

RN 205678-13-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-[(4-aminophenyl)methyl]-2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

RN 205678-14-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-(benzoyl-2-pyridinylamino)propoxy]-2,3,4,5-tetrahydro-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

RN 205678-15-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]propoxy]-2,3,4,5-tetrahydro-2-methyl-3-oxo- (9CI) (CA INDEX NAME)

RN 205678-16-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

RN 205678-17-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[2-(2-amino-4-thiazolyl)ethoxy]-2,3,4,5-tetrahydro-2-methyl-3-oxo- (9CI) (CA INDEX NAME)

RN 205678-18-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4,6-dimethyl-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-2-methyl-3-oxo-(9CI) (CA INDEX NAME)

RN 205678-19-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-3-oxo-8-[3-[(4,5,6,7-tetrahydro-1H-1,3-diazepin-2-yl)amino]propoxy]- (9CI) (CA INDEX NAME)

RN 205678-20-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(3,3-dimethyl-1-oxobutyl)-2-pyridinylamino]propoxy]-2,3,4,5-tetrahydro-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

RN 205678-21-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[[(2-methylpropoxy)carbonyl]-2-pyridinylamino]propoxy]-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

RN 205678-22-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-[[4-(trifluoromethyl)phenyl]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205678-24-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-methyl-2-pyridinyl)amino]propoxy]-3-oxo-2-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

RN 205678-25-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-(methyl-2-pyridinylamino)propoxy]-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

RN. 205678-26-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)-, (4S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205678-27-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205678-28-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-methyl-2-pyridinyl)amino]propoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205678-29-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]propoxy]-2-[[4-(trifluoromethyl)phenyl]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205678-30-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-2-(2-phenylethyl)-8-[3-(2-pyridinylamino)propoxy]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205678-31-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, (4S)- (9CI) (CA INDEX

Absolute stereochemistry.

RN 205678-32-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205678-33-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-, methyl ester (9CI) (CA INDEX NAME)

RN 205678-34-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-3-oxo-8-[3-(2-pyridinylamino)propoxy]-, trifluoroacetate (2:3) (9CI) (CA INDEX NAME)

CM 1

CRN 205677-95-8 CMF C21 H25 N3 O4

CM 2

CRN .76-05-1 CMF C2 H F3 O2

RN 205678-35-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4-amino-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-2-methyl-3-oxo-, trifluoroacetate (2:3) (9CI) (CA INDEX NAME)

CM 1

CRN 205678-02-0 CMF C21 H26 N4 O4

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 205678-36-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4-amino-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

● HCl

RN 205678-37-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl]-2-pyridinylamino]propoxy]-2,3,4,5-tetrahydro-3-oxo-, monosodium salt (9CI) (CA INDEX NAME)

Na

RN 205678-38-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-[[4-(trifluoromethyl)phenyl]methyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 205678-09-7 CMF C28 H28 F3 N3 O4

CRN 76-05-1 CMF C2 H F3 O2

RN 205678-39-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-8-[3-(methyl-2-pyridinylamino)propoxy]-3-oxo-, trifluoroacetate (2:3) (9CI) (CA INDEX NAME)

CM 1

CRN 205678-10-0 CMF C22 H27 N3 O4

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 205678-40-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4;5-tetrahydro-3-oxo-2-(phenylmethyl)-8-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 205678-11-1 CMF C27 H29 N3 O4

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 205678-41-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-[(4-aminophenyl)methyl]-2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 205678-13-3 CMF C27 H30 N4 O4

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 205678-42-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-(benzoyl-2-pyridinylamino)propoxy]-2,3,4,5-tetrahydro-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, trifluoroacetate (20:17) (9CI) (CA INDEX NAME)

CM 1

CRN 205678-14-4 CMF C35 H32 F3 N3 O5

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 205678-43-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]propoxy]-2,3,4,5-tetrahydro-2-methyl-3-oxo-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 205678-15-5 CMF C19 H26 N4 O4

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 205678-44-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[2-(2-amino-4-thiazolyl)ethoxy]-2,3,4,5-tetrahydro-2-methyl-3-oxo-, trifluoroacetate (10:13) (9CI) (CA INDEX NAME)

CM 1

CRN 205678-17-7 CMF C18 H21 N3 O4 S

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 205678-45-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4,6-dimethyl-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-2-methyl-3-oxo-, hydrochloride (2:1) (9CI) (CA INDEX NAME)

●1/2 HCl

RN 205678-46-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-3-oxo-8-[3-(2-pyridinylamino)propoxy]-, ethyl ester (9CI) (CA INDEX NAME)

RN 205678-47-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-[[4-(trifluoromethyl)phenyl]methyl]-, (S)-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 205678-22-4

CMF C28 H28 F3 N3 O4

Absolute stereochemistry. Rotation (-).

CM 2

CRN 76-05-1

CMF C2 H F3 O2

RN 205678-48-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-(methyl-2-pyridinylamino)propoxy]-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 205678-25-7 CMF C29 H30 F3 N3 O4

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 205678-49-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]propoxy]-2-[[4-(trifluoromethyl)phenyl]methyl]-, (S)-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 205678-29-1 CMF C27 H31 F3 N4 O4

Absolute stereochemistry.

CM 2

CRN 76-05-1 CMF C2 H F3 O2

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ΙT
     205676-61-5P 205676-64-8P 205676-65-9P
     205676-66-0P 205676-68-2P 205676-69-3P
     205676-70-6P 205676-71-7P 205676-75-1P
     205676-76-2P 205676-77-3P 205676-78-4P
     205676-79-5P 205676-80-8P 205676-81-9P
     205676-82-0P 205676-91-1P 205676-92-2P
     205677-00-5P 205677-01-6P 205677-02-7P
     205677-03-8P 205677-04-9P 205677-16-3P
     205677-17-4P 205677-18-5P 205677-19-6P
     205677-20-9P 205677-21-0P 205677-22-1P
     205677-23-2P 205677-24-3P 205677-25-4P
     205677-26-5P 205677-28-7P 205677-29-8P
     205677-30-1P 205677-31-2P 205677-32-3P
     205677-33-4P 205677-34-5P 205677-35-6P
     205677-36-7P 205677-37-8P 205677-38-9P
     205677-39-0P 205677-40-3P 205677-41-4P
     205677-42-5P 205677-43-6P 205677-44-7P
     205677-45-8P 205677-46-9P 205677-47-0P
     205677-48-1P 205677-49-2P 205677-50-5P
     205677-51-6P 205677-52-7P 205677-53-8P
     205677-54-9P 205677-55-0P 205677-56-1P
     205677-57-2P 205677-58-3P 205677-59-4P
     205677-60-7P 205677-61-8P 205677-62-9P
     205677-63-0P 205677-64-1P 205677-65-2P
     205677-66-3P 205677-67-4P 205677-68-5P
     205677-69-6P 205677-70-9P 205677-71-0P
     205677-72-1P 205677-73-2P 205677-74-3P
     205677-75-4P 205677-76-5P 205677-77-6P
     205677-78-7P 205677-79-8P 205677-80-1P
     205677-81-2P 205677-82-3P 205677-83-4P
     205677-84-5P 205677-85-6P 205677-86-7P
     205677-87-8P 205677-88-9P 205677-89-0P
     205677-91-4P
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(oxotetrahydrobenzazepine compds. for vitronectin receptor antagonists)

RN 205676-61-5 CAPLUS CN 1H-2-Benzazepine-4-a

1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205676-64-8 CAPLUS

CN Butanedioic acid, [[2-[[bis[(1,1-dimethylethoxy)carbonyl]amino]methyl]-4-methoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 205676-65-9 CAPLUS

CN Butanedioic acid, [[2-(aminomethyl)-4-methoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 205676-66-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205676-68-2 CAPLUS

CN Butanedioic acid, [[2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]methyl]-4-methoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 205676-69-3 CAPLUS

CN Butanedioic acid, 2-[[4-methoxy-2-[(methylamino)methyl]phenyl]methyl]-, 1,4-dimethyl ester (CA INDEX NAME)

RN 205676-70-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-2-methyl-3-oxo-, methyl ester (CA INDEX NAME)

RN 205676-71-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-2-methyl-3-oxo-, methyl ester (CA INDEX NAME)

RN 205676-75-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-2-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

RN 205676-76-2 CAPLUS

CN Butanedioic acid, [[2-[[[(1,1-dimethylethoxy)carbonyl](2,2,2-trifluoroethyl)amino]methyl]-4-methoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 205676-77-3 CAPLUS

CN Butanedioic acid, [[4-methoxy-2-[[(2,2,2-trifluoroethyl)amino]methyl]pheny l]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 205676-78-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 205676-79-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-, methyl ester, (4R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 205676-80-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-, methyl ester, (4S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205676-81-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 205676-82-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205676-91-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[[4-(trifluoromethyl)phenyl]methoxy]-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205676-92-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205677-00-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-2-[[4-

(trifluoromethyl)phenyl]methyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-01-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 205677-02-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 205677-03-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 205677-04-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-)'.

RN 205677-16-3 CAPLUS

· CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-methoxy-3-oxo-2-(2-phenylethyl)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-17-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-hydroxy-3-oxo-2-(2-phenylethyl)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-18-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-19-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-, ethyl ester (9CI) (CA INDEX NAME)

RN 205677-20-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-nitro-1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-21-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4-amino-1-oxido-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-22-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-methoxy-1-

oxido-2-pyridinyl)amino]propoxy]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-23-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-methoxy-2-pyridinyl)amino]propoxy]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-24-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-8-[3-[(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-25-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-3-oxo-8-[3-(2-pyridinylamino)propoxy]-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-26-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl]amino] propoxy]-2,3,4,5-tetrahydro-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-28-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-(3-aminopropoxy)-2,3,4,5-tetrahydro-3-oxo-, methyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 205677-27-6 CMF C16 H22 N2 O4

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 205677-29-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyrimidinylamino)propoxy]-, methyl\_ester (9CI) (CA INDEX NAME)

RN 205677-30-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-31-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[2-(1H-benzimidazol-2-yl)ethoxy]-2,3,4,5-tetrahydro-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{CH}_2-\text{C}\\ \text{O}\\ \text{O}\\ \text{NH} \end{array}$$

RN 205677-32-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-33-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-34-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4,6-dimethyl-1-oxido-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-2-methyl-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-35-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4,6-dimethyl-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-2-methyl-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-36-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[2-(2-amino-4-thiazolyl)ethoxy]-2,3,4,5-tetrahydro-2-methyl-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-37-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-8-[3-[(4-nitro-1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-38-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4-amino-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-2-methyl-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-39-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-nitro-1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-, methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-40-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4-amino-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-, methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-41-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-nitro-1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-42-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4-amino-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-43-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-8-[3-[[[(4-nitrophenyl)methoxy]carbonyl]amino]propoxy]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-44-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-(3-aminopropoxy)-2,3,4,5-tetrahydro-2-methyl-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-45-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]propoxy]-2,3,4,5-tetrahydro-2-methyl-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-46-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-3-oxo-8-[3-[(4,5,6,7-tetrahydro-1H-1,3-diazepin-2-yl)amino]propoxy]-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-47-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-methyl-1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-48-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-methyl-2-pyridinyl)amino]propoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-49-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl]-2-pyridinylamino]propoxy]-2,3,4,5-tetrahydro-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-50-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl](1-oxido-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-51-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl]-2-pyridinylamino]propoxy]-2,3,4,5-tetrahydro-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-52-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-8-[3-[methyl(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-53-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-2-methyl-8-[3-(methyl-2-pyridinylamino)propoxy]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-54-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl](1-oxido-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-2-(phenylmethyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-55-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl]-2-pyridinylamino]propoxy]-2,3,4,5-tetrahydro-3-oxo-2-(phenylmethyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-56-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl]-2-pyridinylamino]propoxy]-2,3,4,5-tetrahydro-3-oxo-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

RN 205677-57-2 CAPLUS

CN  $2H-2-Benzazepine-2,4-diacetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl](1-oxido-2-pyridinyl)amino]propoxy]-1,3,4,5-tetrahydro-3-oxo-, <math>\alpha 2-(1,1-dimethylethyl)$   $\alpha 4-methyl$  ester (9CI) (CA INDEX NAME)

RN 205677-58-3 CAPLUS

CN 2H-2-Benzazepine-2,4-diacetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl]-2-pyridinylamino]propoxy]-1,3,4,5-tetrahydro-3-oxo-,  $\alpha$ 2-(1,1-dimethylethyl)  $\alpha$ 4-methyl ester (9CI) (CA INDEX NAME)

RN 205677-59-4 CAPLUS

CN 2H-2-Benzazepine-2,4-diacetic acid, 1,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-,  $\alpha$ 4-methyl ester (9CI) (CA INDEX NAME)

RN 205677-60-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl](1-oxido-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-2-[(4-nitrophenyl)methyl]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-61-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-[(4-aminophenyl)methyl]-8-[3-[[(1,1-dimethylethoxy)carbonyl]-2-pyridinylamino]propoxy]-2,3,4,5-tetrahydro-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-62-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2-[(4-aminophenyl)methyl]-8-[3-[[(1,1-dimethylethoxy)carbonyl]-2-pyridinylamino]propoxy]-2,3,4,5-tetrahydro-3-oxo-(9CI) (CA INDEX NAME)

RN 205677-63-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-64-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-65-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-(benzoyl-2-pyridinylamino)propoxy]-2,3,4,5-tetrahydro-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-66-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(3,3-dimethyl-1-oxobutyl)(1-oxido-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-67-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[(3,3-dimethyl-1-oxobutyl)-2-pyridinylamino]propoxy]-2,3,4,5-tetrahydro-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-68-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[[(2-methylpropoxy)carbonyl](1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-69-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[[(2-methylpropoxy)carbonyl]-2-pyridinylamino]propoxy]-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-70-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl](1-oxido-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-71-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl](1-oxido-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-72-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl]-2-pyridinylamino]propoxy]-2,3,4,5-tetrahydro-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester, (S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-73-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl]-2-pyridinylamino]propoxy]-2,3,4,5-tetrahydro-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-74-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[[[(4-nitrophenyl)methoxy]carbonyl]amino]propoxy]-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester, (S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-75-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-(3-aminopropoxy)-2,3,4,5-tetrahydro-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$_{\rm F_3C}$$
  $_{\rm MeO}$   $_{\rm O}$   $_{\rm O}$   $_{\rm (CH_2)_3}$   $_{\rm NH_2}$ 

RN 205677-76-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyrimidinylamino)propoxy]-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-77-6 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]propoxy]-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[methyl(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-79-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-(methyl-2-pyridinylamino)propoxy]-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 205677-80-1 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-81-2 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)-(CA INDEX NAME)

Absolute stereochemistry.

RN 205677-82-3 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-83-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-8-[3-(2-pyridinylamino)propoxy]-2-(2,2,2-trifluoroethyl)-, methyl ester, (R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-84-5 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-methyl-1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(4-methyl-2-pyridinyl)amino]propoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-86-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2,2,2-trifluoroethyl)-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-87-8 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[3-[(1-oxido-2-pyridinyl)amino]propoxy]-3-oxo-2-(2-phenylethyl)-, methyl ester, (S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-88-9 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-3-oxo-2-(2-phenylethyl)-8-[3-(2-pyridinylamino)propoxy]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-89-0 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-(2-phenylethyl)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205677-91-4 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 2,3,4,5-tetrahydro-8-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-3-oxo-2-[[4-(trifluoromethyl)phenyl]methyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 205676-89-7P

RL: SPN (Synthetic preparation); PREP (Preparation) (oxotetrahydrobenzazepine compds. for vitronectin receptor antagonists)

RN 205676-89-7 CAPLUS

CN 1H-2-Benzazepine-4-acetic acid, 8-[3-[[(1,1-dimethylethoxy)carbonyl](1-oxido-2-pyridinyl)amino]propoxy]-2,3,4,5-tetrahydro-3-oxo-, methyl ester (9CI) (CA INDEX NAME)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 31 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1985:131794 CAPLUS Full-text

DN 102:131794

TI Total synthesis and study of biologically active lignans. III. Application of the  $\alpha\text{-hydroxyalkylation}$  of  $\beta\text{-benzyl}$   $\gamma\text{-butyrolactones}$  to the preparation of phenyltetralin and bisbenzocyclooctadiene skeletons. First synthesis of picrosteganes, formal synthesis of (±)-steganacin

AU Robin, Jean Pierre; Dhal, Robert; Brown, Eric

CS Lab. Synth. Org., Fac. Sci., Le Mans, 72017, Fr.

SO Tetrahedron (1984), 40(18), 3509-20 CODEN: TETRAB; ISSN: 0040-4020

DT Journal

LA French

AB Kinetically controlled intramol.  $\alpha$ -hydroxyalkylation of a suitable di-Ph aldehyde lactone gave dibenzocyclooctenolactones with a cis lactone-ring junction, such as ( $\pm$ )-picrostegane and ( $\pm$ )-isopicrostegane. Subsequent transformations led to the known ( $\pm$ )-isostegane. The chemical properties, the phys. data and biol. activity of these 3 diastereoisomers were compared with those of ( $\pm$ )-stegane, a 4th diastereoisomer obtained by hydrogenolysis of synthetic ( $\pm$ )-steganacin.

IT 65171-08-6P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

RN 65171-08-6 CAPLUS

CN Butanedioic acid, [[2-(6-cyano-1,3-benzodioxol-5-yl)-3,4,5-trimethoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

IT 65171-03-1

RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with bis(trifluoroacetyl)hydroxylamine)

RN 65171-03-1 CAPLUS

CN Butanedioic acid, [[2-(6-formyl-1,3-benzodioxol-5-yl)-3,4,5-trimethoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

L11 ANSWER 32 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1984:34317 CAPLUS Full-text

DN 100:34317

TI Total synthesis and study of biologically active lignans. Application of the  $\alpha$ -hydroxyalkylation of  $\beta$ -benzyl- $\gamma$ -butyrolactones to the preparation of phenyltetralin and bisbenzocyclooctadiene skeletons. 4. Total synthesis of (±)-steganone and its congeners and synthesis of (±)-stegane

AU Dhal, Robert; Brown, Eric; Robin, Jean Pierre

CS Lab. Synth. Org., Fac. Sci., le Mans, 72017, Fr.

SO Tetrahedron (1983), 39(17), 2787-94 CODEN: TETRAB; ISSN: 0040-4020

DT Journal

LA French

GI

The biphenyl I was cyclized by intramol. hydroxyalkylation to the isomeric alcs. II. These were oxidized using Jones' reagents, to afford the enol together with the  $\beta$ -oxo lactone. Decarboxylation of this mixture using Ba(OH)2, followed by Jones' oxidation gave the isomeric  $\gamma$ -oxo acids which were converted to (±)-steganone (III) using Raphael's method, in an overall yield of 20.7% from the I.

IT 88348-33-8

RL: RCT (Reactant); RACT (Reactant or reagent)(cyclization of)

RN 88348-33-8 CAPLUS

CN Butanedioic acid, [[2-(1,3-benzodioxol-5-yl)-3,4,5-trimethoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

L11 ANSWER 33 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1983:106906 CAPLUS Full-text

DN 98:106906

Total syntheses and studies of biologically active lignans. I. Application of the Ullmann reaction to the preparation of biaryl precursors of bisbenzocyclooctadiene lignans

AU Brown, Eric; Robin, Jean Pierre; Dhal, Robert

CS Lab. Syn. Org., Fac. Sci., Le Mans, 72017, Fr.

SO Tetrahedron (1982), 38(16), 2569-79 CODEN: TETRAB; ISSN: 0040-4020

DT Journal

LA French

GΙ

AB A number of biaryls, with reactive functional groups in the ortho positions, were prepared in ≤88% yield by the Ullmann reaction. E.g., treatment of 2,3,4,5-Br(MeO)3C6HCHO with I in the presence of Cu powder at 210° for 20 min gave 70% II. These biaryls are possible synthons for bisbenzocyclooctadiene lignans such as schizandrin and steganacin.

IT 65171-02-0P 65171-03-1P 84798-99-2P

84799-00-8P

RN 65171-02-0 CAPLUS

CN Butanedioic acid, [(6'-formyl-2',3',4,4',5,6-hexamethoxy[1,1'-biphenyl]-2-yl)methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 65171-03-1 CAPLUS

CN Butanedioic acid, [[2-(6-formyl-1,3-benzodioxol-5-yl)-3,4,5-trimethoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 84798-99-2 CAPLUS

CN Butanedioic acid, [[3,4,5-trimethoxy-2-[6-(methoxycarbonyl)-1,3-benzodioxol-5-yl]phenyl]methyl]-, dimethyl ester, stereoisomer (9CI) (CA INDEX NAME)

RN 84799-00-8 CAPLUS

CN Butanedioic acid, [[3,4,5-trimethoxy-2-[6-(methoxycarbonyl)-1,3-benzodioxol-5-yl]phenyl]methyl]-, dimethyl ester, stereoisomer (9CI) (CA INDEX NAME)

ANSWER 34 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN L11

ΑN 1978:22291 CAPLUS Full-text

DN 88:22291

TΙ Application of the Ullmann reaction to the synthesis of bulky diaryls, precursors of bisbenzocyclooctadiene lignans

ΑU Brown, Eric; Robin, Jean Pierre

CS Lab. Syn. Org., Fac. Sci., Le Mans, Fr.

SO Tetrahedron Letters (1977), (23), 2015-18 CODEN: TELEAY; ISSN: 0040-4039

DT Journal

LA French

GI

AΒ The biphenyl derivs. I [R = CHO, CO2Me, CN, R1 = CH2CH(CO2Me)CH2CO2Me; R = CO2Me, R1 = CHO, CH:C(CO2Me)CH2CO2Me; R = R1 = CHO], potential precursors of steganone and related compds., and II [R = CHO, CH2CH(CO2Me)CH2CO2Me, 5oxotetrahydrofur-3-ylmethyl], potential precursors of schizandrine and analogs, were prepared, mainly by Ullmann reactions. E.g., 2,3,4,5-Br(MeO)3C6HCHO with 2,3,4,5-I(MeO)3C6HCH2CH(CO2Me)CH2CO2Me and powdered Cu at 230° for 0.5 h gave 55% II [R = CH2CH(CO2Me)CH2CO2Me].

ΙT 65171-02-0P 65171-03-1P 65171-06-4P

65171-08-6P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

65171-02-0 CAPLUS

RN

CN Butanedioic acid, [(6'-formyl-2',3',4,4',5,6-hexamethoxy[1,1'-biphenyl]-2yl)methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 65171-03-1 CAPLUS

Butanedioic acid, [[2-(6-formyl-1,3-benzodioxol-5-yl)-3,4,5-CN trimethoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 65171-06-4 CAPLUS

CN Butanedioic acid, [[3,4,5-trimethoxy-2-[6-(methoxycarbonyl)-1,3-benzodioxol-5-yl]phenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 65171-08-6 CAPLUS

CN Butanedioic acid, [[2-(6-cyano-1,3-benzodioxol-5-yl)-3,4,5-trimethoxyphenyl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)

L11 ANSWER 35 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1977:90170 CAPLUS Full-text

DN 86:90170

TI Valonia tannins. V. Trilloic acid, a new phenolic acid from valonia tannins

AU Mayer, Walter; Busath, Harald; Schick, Hartmut

CS Org.-Chem. Inst., Univ. Heidelberg, Heidelberg, Fed. Rep. Ger.

SO Justus Liebigs Annalen der Chemie (1976), (12), 2169-77 CODEN: JLACBF; ISSN: 0075-4617

DT Journal

LA German

GI For diagram(s), see printed CA Issue.

Valolaginic acid (I), a Valonia tannin whose structure was proposed previously (W. Mayer, et al., 1976), yielded on acid hydrolysis ellagic acid and a crystalline compound, trilloic acid trilactone (II). The structures of II and its free acid, named trilloic acid (III), were determined. The acetylated and methylated derivs. of II were prepared. These II derivs. contained an ellagic acid portion linked by C-C bonding with the  $\gamma$ -lactone of a  $\gamma$ -carboxy- $\alpha$ -hydroxyadipic acid. Further 1H NMR studies showed the position of this linkage. The structure of the trilloic acid boundin I was thus determined, and the proposed structure for I was confirmed.

IT 61954-98-1

RL: PROC (Process)

(of Valonia, structure determination of)

RN 61954-98-1 CAPLUS

CN 1,2,4-Butanetricarboxylic acid, 3-(2,6'-dicarboxy-2',3',4,4',5,6-hexahydroxy[1,1'-biphenyl]-3-yl)-4-hydroxy- (9CI) (CA INDEX NAME)

L11 ANSWER 36 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1973:159298 CAPLUS Full-text

DN 78:159298

TI Synthesis of 1-methyl-3-methoxy-7-isopropylnaphthalene

AU Adachi, Kazuo

CS Osaka Inst. Technol., Osaka, Japan

SO Yuki Gosei Kagaku Kyokaishi (1973), 31(2), 166-70 CODEN: YGKKAE; ISSN: 0037-9980

DT Journal

LA Japanese

GI For diagram(s), see printed CA Issue.

The title compound (I) was prepared from m-cresol. Thus, the Grignard reagent of 4-bromo-3-methylanisole was treated with HCHO, condensed with tri-Et ethane-1,1,2-tricarboxylate, hydrolyzed, and decarboxylated to give 81% 2-(4-methoxy-2-methylphenyl)-succinic acid (II). II was refluxed with P2O2 in C6H6 to give 97% 2-(4-methoxy-2-methylbenzyl)succinic acid anhydride (III). The Friedel-Crafts reaction of III in PhNO2-AlCl3 gave 91% 7-methoxy-5-methyl-1-oxo-1,2,3,4-tetrahydronaphthalene-3-carboxylic acid (IV).' Me 6-methoxy-8-methyl-1,2,3,4-tetrahydronaphthalene-2- carboxylate, obtained by the reduction of IV, was treated with MeMgI and decomposed with NH4Cl to give 94% 6-methoxy-8-methyl-2-(1-hydroxy-1- methylethyl)-1,2,3,4-tetrahydronaphthalene (V). V was heated with S to give 59% I.

IT 41499-85-8P

RN 41499-85-8 CAPLUS

CN Butanedioic acid, [(4-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{MeO} \\ \hline \\ \text{CH}_2-\text{CH}-\text{CH}_2-\text{CO}_2\text{H} \end{array}$$

=> d 12; d 17; d his; log y L2 HAS NO ANSWERS L1 STR

Structure attributes must be viewed using STN Express query preparation. L2 QUE ABB=ON PLU=ON L1

L7 HAS NO ANSWERS L6 STR

$$\begin{array}{c} \circ \\ \\ \end{array}$$

Structure attributes must be viewed using STN Express query preparation. QUE ABB=ON PLU=ON L6 L7 (FILE 'HOME' ENTERED AT 14:13:57 ON 11 AUG 2007) FILE 'REGISTRY' ENTERED AT 14:14:17 ON 11 AUG 2007 L1STRUCTURE UPLOADED L2 QUE L1 L3 1 S L2 28 S L2 FUL L4FILE 'CAPLUS' ENTERED AT 14:14:48 ON 11 AUG 2007 L5 15 S L4 FILE 'STNGUIDE' ENTERED AT 14:14:56 ON 11 AUG 2007 FILE 'REGISTRY' ENTERED AT 14:16:34 ON 11 AUG 2007 STRUCTURE UPLOADED L6 L7 QUE L6 . 8 S L7  $^{L8}$ L9191 S L7 FUL FILE 'CAPLUS' ENTERED AT 14:18:12 ON 11 AUG 2007 L10 29 S L9 36 S.L5 OR L10 COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 708.74 191.13 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) TOTAL SINCE FILE ENTRY SESSION CA SUBSCRIBER PRICE -28.08 -28.08

STN INTERNATIONAL LOGOFF AT 14:19:51 ON 11 AUG 2007